An investigation of the effects of coordination training on cognitive function in older adults

by

Iseult Anna Cremen, B.A.

A dissertation submitted to the

University of Dublin, Trinity College Dublin

for the degree of

Doctor of Philosophy

in the

School of Psychology

Trinity College Dublin

Dublin, Ireland.

November, 2017

Declaration

I, Iseult Cremen, confirm that this thesis has not been submitted as an exercise for a degree at this or any other university and is entirely my own work.

I agree to deposit this thesis in the University's open access institutional repository or allow the Library to do so on my behalf, subject to Irish Copyright Legislation and Trinity College Library conditions of use and acknowledgement.

Signed,

Iseult A. Cremen

November 24th, 2017

Abstract

The world's population is ageing. It is well known that the ageing process causes progressive loss of various cognitive functions and physical capacities. Modern neuroimaging techniques have shown that these changes are associated with structural brain changes. Diminished cognitive function in old age is not however universal. The actual loss of function differs greatly between individuals. The finding that neuroplasticity, the brain's capacity for adaptive reorganisation and change, is retained in the ageing brain has inspired much research looking into methods to ameliorate cognitive decline amongst older adults. Research has shown that certain lifestyle factors are related to better cognitive health, such as level of education, socioeconomic status social engagement, habitual levels of physical activity, and occupational attainment. Of these factors, only a few are currently thought to be amenable to change in later life. As a consequence, a great deal of research over the past two decades has focussed on the use of interventions with a view to enhancing cognitive function in older adults, and preventing further decline. Cognitive training interventions that focus upon specific components of cognitive function have not lived up to their initial promise. In particular, there is little evidence that any derived benefits extend to capabilities that have not been trained directly. In this regard, physical activity interventions appear to have greater potential. Engaging in aerobic physical activity has been shown to provide benefits for the ageing brain; however, little is known about the underlying mechanisms subserving these benefits. There has been some recognition that multiple 'pathways' mediate the benefits for cognition that accrue from different types of physical activity. That which has been neglected to date is consideration of "motor fitness" – components of physical capability distinct from muscle strength and cardiovascular capacity – which are linked to the retention of cognitive function. In this regard, associations have been shown between executive function and key elements of motor fitness, such as movement speed, balance, and motor coordination.

The factors that account for the generalised effects of motor fitness on cognitive function are not currently understood, and have not yet been examined in detail. In order to exploit its therapeutic potential, this deficiency must be addressed. The purpose of the present work is to explore the effects of motor coordination training on the executive functions of older adults. Chapter 1 is a review of the literature that provides the theoretical basis for the experimental work reported in this thesis. The latter comprises

two blinded randomised controlled trials that explore the impact of two variants of motor coordination training on the cognitive function of older adults.

In the first study (Chapter 2), twenty healthy older adults trained individually on a unilateral centre-out target acquisition task in five sessions conducted over one week. A second group of twenty participants were engaged in an active control task. Executive functions were assessed prior to training, post-intervention and at a retention session conducted ten days following the post-test. Individuals who engaged in the motor training task exhibited improvements on a subset of the cognitive tasks, including the Choice Reaction Time task and components of the Dual n-Back task. These improvements in performance were not exhibited by individuals who engaged in an active control task. In addition, all participants carried out a visuomotor task at the pre- and post-intervention sessions. Individuals who were engaged in the motor training task exhibited improved performance on the visuomotor task post-intervention, in terms of decreased movement time and lower path deviation, whereas these effects were not observed for control group participants. In addition, interlimb transfer from the trained limb to the untrained limb was observed on the baseline motor task post-intervention for the training group only, indicating that neural adaptation to the motor task occurred. However, no association was found between individual degree of adaptation to the baseline motor task and the degree of improvement on the cognitive measures.

In the second trial (Chapter 3) thirty older adults were trained individually on a different variant of the target acquisition task in which the visual feedback was deferred, A second group of thirty participants were engaged in an active control task. Provision of post-trial feedback is thought to engender 'explicit' learning strategies in task adaptation. Individuals who were engaged in the motor training task exhibited improved performance on components of the Wisconsin Card Sorting Task (WCST). In addition, all participants carried out a visuomotor task at the pre- and post-intervention sessions. Individuals who were engaged in the motor training task exhibited differences in performance on the visuomotor task at the post-intervention session, showing decreased velocity and later time at peak velocity at the post-test, and lower path deviation at the retention session, whereas these effects were not observed for control group participants. In addition, interlimb transfer from the trained limb to the untrained limb was observed in performance on the visuomotor task at post-intervention for the motor training group only, providing additional evidence that neural adaptation to the motor task occurred. In addition, these participants showed a degree of improvement on the Trail Making Task and the Mental Rotation Task. A statistical relationship was found between the degree of

adaptation to the visuomotor task at the post-intervention session and the number of Conceptual Level Responses on the WCST. This suggests common mediation of the alterations in motor control that were brought about through repetition of the coordination training task, and the gains in cognitive function that were observed following the cessation of training.

Finally, Chapter 4 provides a discussion of the findings and their implications, along with future challenges in this avenue of research. In general summary, the results of the randomised controlled interventions described herein support the proposition that motor training can lead to positive transfer of functional capacity to the cognitive domain.

Acknowledgements

First and foremost, I owe my sincerest gratitude to my supervisor, Professor Richard Carson. His continued support and guidance made it possible for me to complete this work. Thank you for your patience and encouragement. It was wonderful to work in an environment that taught me to question everything, always find a better way, and to keep searching for ways to improve research.

I would also like to thank the other members of staff in TCIN, the School of Psychology and School of Engineering who assisted me along the way, with technical issues, employment, guidance and inspiration. It was a pleasure to work in such a stimulating environment.

Thank you to the other members, past and present, of the Carson lab: Kathy, Emmet and especially Dave Bolton, who assisted greatly in the early days of the project, and continues to provide help from afar. Thank you Megan, Alex, Nadja, Alex, Anna, Stefan, Roisin and Antonio: your great humour and ever-inquisitive minds made research exciting and fresh. Spending well over 1000 hours collecting data would certainly not have been bearable without your company (and international cake-making skills).

Thank you to the many research assistants, who gave up their time to assist with data collection: Virginia, Eva, Micheli, Celine, Aifric, Maeve, Caoimhe, Laura, Alice, Nadine, Taryn and Jessica. Without your help, experimental blinding would have been impossible, and the overall quality of the research would no doubt have suffered. I must also give my sincerest thanks to the participants who gave up their valuable time to participate in my study: it was a pleasure to work with you all and not only did you provide me with my data, but offered many valuable insights into life and ageing.

I would like to thank the Irish Research Council for providing me with funding to carry out this project.

Thank you to my fellow PhD colleagues, who have provided endless conversations and help with all and any research issues, in particular Katie, Sadhbh, Lisa, Shane, Jen, and everyone in the NEIL office, the O'Connell Lab, and the Dockree Lab: you brightened up the long hours in TCIN, and I am proud to call many of you my friends.

I must thank my wonderful friends and family, especially Adam, for believing in me even when I was having trouble believing in myself. And finally, to my wonderful

Mom and Dad, who have supported me at every step along this path (from Playschool to PhD!)- thank you.

ISEULT A. CREMEN

Trinity College Dublin
November 2017

Table of Contents

Glossary of Abbreviations

ALE- Activation Likelihood Estimation

AUT- Alternative Uses Task

BDNF- Brain-Derived Neurotrophic Factor

CLR- Conceptual Level Response

CNS- Central Nervous System

CRT- Choice Reaction Time Task

DIC- Deviance Information Criterion

DLPFC- Dorsolateral Prefrontal Cortex

EEG- Electroencephalography

EF- Executive Function

Ext - Extension

Ext-Rad- Extension-Radial

Ext-Uln – Extension-Ulnar

Flx- Flexion

Flx-Rad- Flexion-Radial

Flx-Uln – Flexion-Ulnar

fMRI- functional Magnetic Resonance Imaging

GLMM- Generalised Linear Mixed Model

GMA- Gross Motor Activities

HAROLD- Hemispheric Asymmetry Reduction in OLDer adults

HDI- Highest Density Interval

HE- Heading Error

Hz- Hertz

IGF-1 – Insulin Growth Factor-1

IQR- Inter Quartile Range

LED- Light Emitting Diode

LH- Left Hand

M1- Primary Motor Cortex

MCMC- Markov Chain Monte Carlo

MCT- Multi-Component Training

MEP- Motor Evoked Potential

MMSE- Mini Mental State Exam

MoCA- Montreal Cognitive Assessment

MT- Movement Time

MTL- Medial Temporal Lobes

MVPA- Multi Voxel Pattern Analysis

PA- Physical Activity

PB- Percentage Bend

PD- Path Deviation

PFC- Prefrontal Cortex

PV- Peak Velocity

PVT- Time at Peak Velocity

QMT- Quadrato Motor Training

Rad - Radial

RH- Right Hand

RT- Reaction Time

SAL- Spectral Arc Length

SART- Sustained Attention to Response Task

SD- Standard Deviation

SE- Standard Error

SMA- Supplementary Motor Area

SMT- Simple Motor Training

TMS- Transcranial Magnetic Stimulation

TMT- Trail Making Task

TUG- Timed Up and Go

Uln- Ulnar

VM- Visuomotor

VT- Verbal Training

WCST- Wisconsin Card Sorting Task

WM- Working Memory

Chapter 1 Can motor training interventions lead to enhanced cognitive function in older adults?

1.1 Introduction

It is well known that the ageing process causes changes in the brain (Raz et al., 2005). These changes may in some cases result in a progressive loss of cognitive function (Nyberg et al., 2012; Raz and Rodigue, 2006). In addition, age is a major risk factor for a number of neurodegenerative disorders including Alzheimer's disease (Lindsay et al, 2002). Globally, the number of older adults (aged 60+) is growing faster than any other age group, and this group is expected to double in size from 901 million in 2015 to nearly 2.1 billion by 2050 (UN World Population Ageing, 2015). Ageing and its associated declines pose a challenge to modern society, placing increasing stress on healthcare systems. As cognitive decline has emerged as one of the biggest health threats of old age (e.g. Bishop, Lu, & Yankner, 2010; Plassman et al., 2008), it is imperative to identify strategies to prolong independent living, prevent cognitive decline and enhance quality of life for the elderly. There is a need to identify valid, cost-effective interventions which serve to preserve cognitive capacities, prevent or delay further decline and even improve declining capacities (Kueider et al., 2012). However, diminished cognitive function in old age is neither uniform nor universal (Deary et al., 2009). An encouraging line of research has established that neural plasticity, the brain's capacity for adaptive reorganization and change, is maintained in the ageing brain (Burke & Barnes, 2006; Grady, 2012; Gutchess, 2014). Despite the inevitability of a certain level of functional decline with age (e.g. Spiruduso, Francis & Macrae, 1995), the extent of these losses vary enormously between individuals (Deary et al., 2009), even amongst those showing evidence of neurodegeneration (Horn, 1986; Ince, 2001; Katzman et al., 1998; Stern, 2002). There are many intrinsic and environmental factors which may explain this variation, including: the period of time spent in education, occupational attainment, socioeconomic status, degree of social engagement, and habitual levels of physical activity (e.g. Bezerra et al., 2012; Scarmeas et al., 2001; Stern et al., 1994; Yaffe et al., 2009). Of these factors, only a few are amenable to modification in later life. As a consequence, a great deal of research has focussed on interventions such as cognitive training (e.g. Tardif & Simard, 2011; Nouchi et al, 2012) and aerobic exercise (e.g.

Colcombe & Kramer, 2003; Busse, Gil, Santarém & Filho, 2009; Kramer, Erickson & Colcombe, 2006), with a view to ameliorating loss of cognitive function in older adults.

However, attempts to employ 'cognitive training' or 'brain training' programmes have shown limited efficacy, particularly in their failure to show improvements on measures unrelated to the training task, or to 'real world' cognitive skills (Lampit et al., 2014; Melby-Lervag et al., 2016; Owen et al., 2010; Simons et al., 2016; Souders et al., 2017). The ontologies of cognitive function and cognitive ageing upon which these interventions have been developed have characterised cognition as modular, computational, localised and representational (e.g. the ACTIVE Trial, Jobe, 2001; Jaeggi, Buschkuehl, Jonides & Perrig, 2008). Indeed, therapeutic interventions in which a specific component of cognition is targeted are predicated on a modular view of cognitive capacity, and the corresponding belief that certain faculties decline in isolation. For example, there are a host of cognitive training interventions that have tried to specifically improve working memory (e.g., Jaeggi, et al, 2008; Guye & von Bastien, 2017; Toril et al., 2016, for reviews see Melby-Lervag & Hume, 2013; Shipstead, Redick & Engle, 2012). While there is accumulating evidence that the ageing process differentially affects particular brain regions (Raz et al., 2005), the distribution of degenerative change is not "diffuse, random or confluent" (Seeley et al., 2009, p.49). Rather, it follows an orderly and sequential process, affecting brain networks that mediate functionally related processes (Carson, 2017). These networks tend not to align with the modular architecture that is an element of traditional models of cognitive function (e.g. Anderson, 2010). Thus, in order to harness the potential benefits of neural plasticity, it is time for an alternative ontology of cognition, that encourages a more holistic and integrated view of cognition as is supported by data from neuroimaging studies (e.g. Uttal, 2013). This will permit novel methodologies to be developed in attempts to enhance cognitive function in older adults.

1.2 Neural Reuse and an Enactive View of Cognition

> *"The brain is an action-oriented, and not a perception-oriented, system. It is crucial to understand the implications of this fact for the nature of the brain and for the science that purports to study it."* (Anderson, 2016; p125).

The predominant characterisation in traditional cognitive science is of cognition as a computational system in which perception is conceived as reconstructive and symbolic (Churchland & Sejnowski, 1994; Fodor, 1981; Marr, 1982; Neisser, 1976; Newell & Simon, 1972). Perception is regarded as the informational input to the computational cognitive system, which translates incoming information into symbolic representations, which the cognitive system manipulates and modifies in order to guide motor actions. In this traditional cognitive science depiction of cognition, representation is central. Our sensory organs notionally provide us with incomplete, fragmented information about the world, from which we generate models of the true nature of the world. These models are tested and refined with further incoming sensory data. Only then can cognition begin; we use these models to form beliefs, reason about them, use them to make decisions, etc. Anderson (2016) notes that this view of cognition is "postperceptual—even in some sense aperceptual—representation-rich and deeply de-coupled from the environment" (p.164). Under this ontology of cognition, attempts to describe cognitive function thus target this 'post-perceptual' representational system.

In addition, with the advent of novel neuroimaging techniques, a significant body of cognitive neuroscience research has focussed on demarcating the specific cognitive functions that are represented in different areas of the brain (Rypma & D'Esposito, 1999; Shallice, Fletcher, Frith et al., 1994; Paulesu, Frith & Frackowiak, 1993). In the cognitive neuroscience of ageing, the focus has often been on brain regions that might be related to decline in specific cognitive functions (e.g. Cabeza et al., 2004; de Fockert, Rees, Frith, & Lavie, 2001; Grady et al., 1998). It follows logically from this epistemic position that attempts to enhance cognition, such as working memory training, should target specific 'higher-order' processes that control the reconstructed representations and symbols that are purportedly the currency of our cognitive systems.

The pervasive view of the mind as a symbol system (Vera & Simon, 1993) allows for the clean separation of perception, cognition and action. Given its dominant position, this view has tended to shape the manner in which evidence derived from sources such

as brain imaging, has been integrated by those seeking to understand age-related changes in behaviour and functional capacity. It might thus appear natural to focus investigation of the brain on the componential physical apparatus underlying such a system. There is however also an emerging 'pragmatic turn' in cognitive science away from representational models and towards 'enactive' models that place action at the centre of cognition (Engel, Maye, Kurthen and Konig, 2013; Gibson, 1966; O'Regan & Noe, 2001), or more specifically, that cognition is ('embodied') action (Varela, Thompson & Rosch, 1991). The term 'embodied' emphasises the recognition that our cognition depends on the bodies that we possess, endowed as they are with specific sensorimotor capacities, embedded in our particular biological, psychological and cultural environment. A full philosophical account of 'embodied cognitive science' is beyond the scope of this thesis. There is a vast discourse in this area, which spans the domains of philosophy, psychology, cognitive science, sports science and neurophysiology among others (for a recent précis, see Anderson, 2016). But central to this 'enactive' position is the idea of cognition as the capacity to generate structure by action (Engel et al., 2013), and further that cognitive functioning cannot be separate from embodiment. Common across motor theories of cognition is the idea that the brain evolved not for the purpose of cognition and thinking, but for adaptive action situated in the environment (Koziol et al., 2014). They go beyond merely stating that cognition and action are dependently linked; but rather extend to the proposition that there is no duality between motor and cognitive functions, and that they are more appropriately considered as having evolved together (Koziol et al., 2011; Bloedel & Bracha, 1997).

1.2.1.1 Shared Evolution of Motor and Cognitive Functions

Despite the traditional conceptualisation of motor and cognitive systems as functionally distinct, recent work has drawn attention to the shared evolution of these systems. A recent review by Mendoza and Merchant (2014) on the shared evolution of cognitive and motor functions outlines a compelling perspective showing that the evolutionary emergence of complex motor cortical areas, such as is seen in the frontal lobes of primates, allows for greater flexibility of movement and behaviour that is not seen in any other mammalian group. Closely correlated with the emergence of these highly evolved motor control regions is the emergence of 'higher-order' cognitive functions. Similarly, it has been argued that certain 'cognitive' functions have evolved to serve motor control, such as executive functions (Koziol et al, 2011; Stout, 2010); working memory (Carruthers, 2013); and selective attention (Vallortigara, Rogers &

Bizarra, 1999). In addition, Pezzulo (2011) argues that the mechanisms engaged in sensorimotor learning over the course of evolution were reused in the emergence of cognitive processes. It is suggested that procedural knowledge developed as an outcome of mechanisms used to control and execute actions, and that declarative knowledge developed through mental simulation of re-enactment of such behaviours. More recently, a related class of theories emphasising re-use of the neural architecture involved in the control and generation of actions as the basis upon which higher-order cognitive processes emerged, have been subject to increasing empirical scrutiny.

1.2.1.2 Neural Reuse

The enactive view promotes a holistic account of the architecture of our cognitive systems. In contrast to evolutionary psychology's proposition that the brain is composed of "special purpose neural modules" (2016, p120), Anderson's 'neural reuse' theory posits that individual neural components are used and reused for various cognitive and behavioural objectives, with diverse neural elements cooperating with different partners and overlapping regions, or 'neural coalitions' to carry out behaviours. In essence, the same finite reserve of neural resources are used and reused in multiple ways as needed. Anderson (2014) outlines a range of evidence in support of neural reuse, including studies that combine and re-examine data from hundreds of neuroimaging experiments to show that nearly all regions of the brain are functionally diverse and highly integrated (Anderson, 2007; Anderson et al., 2013); single-neuron recording studies showing that neurons have mixed selectivity (Cisek 2007; Cisek & Kalaska 2005; 2010); sensory substitution studies (Merabetet al. 2008), and other examples spanning the cognitive neuroscience literature that are more consistent with the theory of neural reuse than traditional componential models. It is not thought that the entire brain is involved in every cognitive process; an important distinction is drawn between functional differentiation and functional specialisation. While there is functional differentiation, networks are also intricately integrated. Separate brain networks share elements, but the elements may have a different purpose for the different networks in which they are a part. The key implication of this theory is that, rather than having been supported by targeted adaptations, the evolution of "higher-order" cognitive processes has been promoted by the utilisation of existing neural resources and behavioural strategies.

This enactive view now needs to be extended to our epistemic position concerning the study of cognitive ageing and enhancement. If, as many are now suggesting (e.g. Anderson 2014; 2016; Anderson & Chemero, 2016; McGann, 2007;

Varela et al., 1991), the brain has evolved to control action and manage agent-environment relationships, we can look at cognitive decline with age as a decline in the ability to engage with and adapt to the environment. Actions do not simply refer to biological movements of the body, actions are 'intentional' i.e. they are goal-driven, and involve planning, decision-making, and prediction of intended outcomes, and which may be associated with a sense of agency (Wilson & Shpall, 2016). Attempts to improve isolated components of cognitive function have yielded disappointing results over the past decade (e.g. Lampit et al., 2014; Melby-Lervag et al., 2013). Training on specialised cognitive tasks in order to improve a specific function has largely been an unsuccessful avenue of research. Although meta-analyses have shown small improvements on measures of intermediate transfer to untrained tasks following cognitive training, there is little evidence of transfer to 'real world' cognitive skills (Lampit et al., 2014; Melby-Lervag et al., 2016; Owen et al., 2010; Simons et al., 2016; Souders et al., 2017). Diamond and Ling (2016) looked at 84 intervention studies attempting to improve EFs, including computerized training, games, aerobic exercise, resistance training, martial arts, yoga, mindfulness, theatre, school curricula. It was concluded that transfer from EF training does occur, but is 'narrow' transfer; people only improve on what they practice. As Druin Burch noted: "Doing something repeatedly can make you better at it, which is not the same as saying it makes you better" (2014, p.2). This mode of intervention is a logical methodological solution to the information the cognitive neuroscience of ageing has provided over the past three decades. Thus, in light of both philosophical and empirical considerations, it might be concluded that in attempting to enhance cognitive function, the modular assumption of the brain is not the most advantageous in terms of guiding interventions. Perhaps it is time to step back and re-evaluate not only the specific method of intervention, but also the conceptualisation of cognitive functions as arising from localised patterns of brain activity. In its stead, alternative ontologies of cognition may in turn also proffer novel methodologies for the amelioration of cognitive decline. Moreover, they may help to redefine epistemic ideas on what constitutes enhanced function. Following the enactive turn in cognitive science and Anderson's neural reuse theory, a person's ability to control their actions and interact with and adapt to its environment should be central to interventions and the measurement of their success. In addition, this action-centred approach should be used to guide our interpretation of the valuable information that brain imaging has given us in recent decades.

1.3 Age-Related Changes in the Brain and Cognition

There is general consensus, unsurprisingly, that a certain level of decline in cognitive function is considered a normal feature of ageing (e.g. Spirduso & MacRae, 1995). Whilst this has been widely accepted for hundreds of years (see Cokayne, 2003 for an account of old age in Ancient Rome), the deployment of functional magnetic resonance imaging (fMRI) in the 1990s has generated many additional insights into cognitive ageing. An explosion of research looking at the structure and function of the ageing brain has occurred. Decline in cognitive function is attributed to a host of changes in the structure and function of the brain (Deary et al., 2009). It has been shown that overall brain volume declines with age, due to reduced grey matter volume (Courchesne et al, 2000; Good et al., 2001; Gunning-Dixon et al., 1998; Jernigan et al 2001; Raz et al 1997; Resnick et al 2003; Salat et al., 2004; Sowell et al., 2003), particularly in prefrontal areas (Raz et al, 2004), primarily due to reductions in dendritic branches and synaptic connections rather than neuronal losses (Fjell & Walhovd, 2010). White matter volume and density exhibit declines later but at a more accelerated rate (Courchesne et al., 2000; Ge et al, 2002; Jernigan et al, 2001). Increased ventricle size also contributes to lower volume (Davis & Wright, 1977). Changes are also seen in reduced efficiency in neurotransmitter function (Hillman, Buck & Thelmanson, 2009). While losses due to age are widespread in the brain (Raz, 2000), the frontal cortex, basal ganglia and hippocampus and associated medial temporal lobe areas are the most susceptible areas to age-related decrements (Buckner, Head & Lustig, 2006; Raz and Rodrigue, 2006), with the prefrontal cortex (PFC) and medial temporal lobes (MTL) showing greatest losses (Haug & Eggers, 1991; Raz, 2000).

These changes of the brain and central nervous system are associated with decreasing proficiency in cognitively demanding behaviours and are thought to be responsible for age-related declines in cognitive function (Bamidis, 2014; Duan et al, 2003; Morrison and Baxter, 2012; Nyberg et al., 2012; Reuter-Lorenz & Park, 2014; Stern, 2009). Thus, the cognitive functions with greatest reliance on the areas of the brain most susceptible to degeneration, i.e. the PFC and MTL areas, are thought to be the most vulnerable to decline (Burke & Barnes, 2006); and indeed this is manifested as an accelerating decline in behaviours that are purportedly regulated by these regions (Nyberg et al., 2012; Ronnlund, Nyberg and Backman, 2005; Park et al., 2002; Salthouse, Atkinson & Berish, 2003), including processing speed, executive function and episodic memory (Horn, 1986). Much work has used fMRI to identify neural activity patterns

occurring during the performance of specific cognitive tasks, and the activated areas are then designated as functionally specific, and labelled according to the corresponding task demands. Following this, differences in these regions during task performance between young and older adults are compared. If older adults show decrements in these tasks, and corresponding differentiated brain activity patterns, they are labelled as functions 'in decline'. Comparisons between older and younger adults have consistently found age-related declines in tasks involving executive functions (e.g. inhibitory control, attentional control, processing speed and working memory) and long-term/ episodic memory (Kramer, Erikson & Colcombe, 2006; Glisky, 2007; Park et al., 2001; Bamidis et al, 2014). Sustained attention and inhibitory control processes, functions thought to be reliant on regions in the prefrontal cortex, also show age-related deficits (Chao & Knight, 1997; West, 1996). Reduced connectivity is seen between frontal and posterior brain regions, and this has been suggested as an explanation for reduced attentional capabilities (Grady, 2012).

It has long been recognised that motor functions also exhibit declines in 'healthy' (non-pathological) ageing (e.g. Ketcham, Stelmach, Birren, & Schaie, 2001; Seidler and Stelmach, 1995; Spirduso, 1975; Welford, 1988). Documented behavioural changes in motor functions include difficulty with coordination of movements (Seidler et al., 2002; 2010), greater spatial and temporal variability of movement (Contreras-Vidal et al., 1998; Darling et al., 1989), general slowing of movements (Buckles, 1993), processing speed decrements (Salthouse, 2000), gait and balance difficulties (Tang and Woollacott, 1996) and the declining ability to inhibit actions (Levin et al., 2014). Sensorimotor cortex volume has been associated with differences in gait in older adults (Rosano et al, 2008), and cerebellar volume has been linked to motor and functional declines (Bernard and Seidler, 2014). Changes in the action of neurotransmitters in comparison to younger adults have also been associated with motor declines, with differences in cholinergic, serotonergic and noradrenergic systems potentially leading to declines in motor abilities (Gottfries, 1990; Kaasinen and Rinne, 2002; Cham et al, 2007; 2008). As is the case for age-related cognitive declines, the literature dealing with age-related changes in motor function is vast (e.g. Mattay et al., 2002; Spirduso & MacRae, 1990; Spirduso, Francis & MacRae, 1995).

Whilst there has evidently been a great amount of research exploring both cognitive and motor declines and their neural correlates, a principal concern is that these literatures have remained almost entirely distinct. Novel brain imaging technologies have allowed us to explore neural function in a way not previously possible, however the

interpretation of this literature has led to two largely separated fields of research. Even within the motor and cognitive research domains, research often explores segregated regions of the brain in isolation, a natural result of the 'traditional' computational model of the brain. The schismatic way that this brain imaging data has been interpreted has in turn had a huge impact both on the models of cognitive decline that have been applied in seeking to capture the causes and processes that underlie cognitive ageing, and the strategies of remediation that have been promoted as a consequence.

1.3.1 Theories of Cognitive Decline: Common Cause Hypotheses, De-differentiation and Compensation

Although at first glance, brain imaging data have provided observations at additional levels of description that appear to support prevailing theories of cognitive decline, specific interpretations of the evidence have varied widely. Certain 'common cause' hypotheses claim that a deficit in one brain mechanism is responsible for a broad class of functional decline manifested in older adults, e.g. inhibitory functions (Hasher & Zacks, 1988), slower information processing (Salthouse, 1996; Sleimen-Malkoun, Temprado and Berton, 2013), cognitive control (Botvinick et al., 2001; Braver & Barch, 2002) or sensory functions (Baltes and Lindenberger 1997). The view that one functionally distinct brain mechanism subserves all functional decline with age, is plausible under the traditional cognitive science view of cognition: it is analogous to one component in a computer processing system breaking down and consequentially, processes coming "later" in the sequence suffering the consequences. In the brain, it is as if the perceptual input has reached the cognitive 'symbol manipulation' system, but that a processing deficit means that the behavioural output of the cognitive system, the actions, are impaired as a consequence.

Viewed critically, however, it can be argued that neuroimaging data provides evidence that is more consistent with a holistic conception of decline. On the basis of the observation that brain activation patterns in older adults are recognisably different from those of young adults, the 'de-differentiation' hypothesis of ageing posits that as we age, cognitive tasks increasingly depend on spreading activation and shared neural substrates (Li, Lindenberger and Sikstrom, 2001; Park et al., 2004). In comparison with younger people, older adults show increased activation in 'task-specific' brain regions, recruit additional brain areas ('unique recruitment') and even use completely different brain regions ('substitution') when performing cognitive tasks (Park et al., 2001). For example,

Reuter-Lorenz, Stanczak and Miller (1999) used functional magnetic resonance imaging (fMRI) to demonstrate that older adults display less lateralization of function when performing cognitive tasks (physical identity tasks of varying levels of complexity). Some researchers have framed different activation patterns in older adults as compensatory mechanisms (e.g. Reuter-Lorenz et al., 2000; Davis et al., 2008; Vallisi et al, 2011). Cabeza and colleagues (2002) put forward the model of hemispheric asymmetry reduction in older adults (HAROLD), having inferred that higher performing older adults compensated for age-related decrements in cognitive task performance by recruiting inter-hemispheric regions. Bilateral recruitment was associated with improved task performance. In contrast, lower performing older adults engaged only one hemisphere (Park & Reuter-Lorenz, 2009), as did successfully performing younger adults. It is thought that this 'compensation' is mediated by a plastic reorganisation of neural networks in the high-performing ageing brain.

As a brief aside, while many studies relate increased activity in certain brain regions to improved task performance in older adults, increased activation and de-differentiation may not always be compensatory in nature - it is likely dependent on task and response parameters (Grady, 2012). For example, deChastelaine and colleagues (2011) found that greater PFC activity in memory tasks was related to poorer performance. Elsewhere, Morcom, Li and Rugg (2007) looked at memory performance on a retrieval task, matching performance levels between groups of older and younger adults. Using fMRI, they observed that older adults recruited regions more extensively and had fewer task-related activity reductions. They suggested that the most parsimonious explanation is that older adults show declining neural efficiency when engaging in cognitive activities. Thus, it is likely that activation patterns, and whether they are compensatory or associated with poorer performance, are task-dependant. What is important in this context is that widespread patterns of activation in the brain are different in older adults; not just activity in specific, localised regions.

Whereas compensation and de-differentiation theories have primarily been supported using evidence from cognitive tasks, a number of studies now suggest that during motor task performance, similar phenomena are evident. One study, using multi-voxel pattern analysis (MVPA) to compare activation patterns of "motor representations" in younger and older adults, found that the distinctiveness of neural representations was reduced in older adults throughout the motor control network (M1, SMA, insula and cerebellum) (Carp et al., 2011). It is becoming clear therefore that de-differentiation in older adults can be seen in motor networks. Heuninckx and colleagues (2005) used fMRI

to demonstrate that participants recruited additional brain regions in the performance of wrist movements, along with the typical networks activated in younger adults. With the most complex tasks, additional activation was seen in anterior rostral cingulate and dorsolateral prefrontal cortex (DLPFC), areas involved in inhibitory cognitive control. Later studies by Heuninckx and colleagues (2008) found that additional recruitment was positively correlated with motor performance in older adults, which is consistent with the compensation hypothesis. Reuter, Behrens and Zschorlich (2015) have recently shown that during planning of wrist movements, motor evoked potentials (MEPs) were less specifically modulated in older adults. They concluded that amongst older adults, de-differentiated activation of the primary motor cortex during movement preparation might be partly responsible for poorer motor control.

As is evidenced from the research outlined above, the interpretation of fMRI data (along with those derived from other methodologies), and in particular the degree to which they are interrogated in terms of the activity that is registered in closely circumscribed brain regions, as opposed to more widely distributed brain networks, can lead to quite different explanations of cognitive ageing. Certain models of cognitive function and cognitive ageing that have become popular in the advent of neuroimaging technologies have focussed on decline in highly specific regions of the brain, and are associated with a view of cognition that is modular and computational. This modular view of cognitive capacities can lead to the belief that certain functions decline in isolation; and that these may even be solely responsible for widespread decline (e.g. Salthouse, 1996; Hasher & Zacks, 1988). Alternative models, such as those that concern de-differentiation and compensation mechanisms lead more naturally to consideration of common mechanisms that may mediate multiple facets of motor control and cognition. Nonetheless, the modular view remains the most widely adopted and accepted framework. As a consequence, the most pervasive interventions are those that have as their target a specific component of cognition that has been designated through a conjunction of behavioural assessment and brain imaging. For example, many cognitive interventions have used ‘working memory training’ in attempts to specifically improve working memory (see reviews by Melby-Lervag & Hume, 2013; Morrison & Chien, 2011; Shipstead, Redick & Engle, 2012).

1.3.2 A Closer Look at Executive Function

Attempts to improve cognitive functioning in older adults commonly focus on executive functions, not only as these functions are understood to be most susceptible to

decline, but in addition they have been associated with a number of outcomes that are thought to indicate 'success' in modern society. EFs have been proposed to be predictive of health, success in both school and workplace settings, and quality of life throughout the ages (e.g. Duckworth and Seligman, 2005; Moffitt et al., 2011; Bailey, 2007). Executive function is a blanket term that has been used to describe higher-level cognitive functions involved in the control of 'lower-level' processes and goal-directed behaviours (Alvarez and Emory, 2006).

It has been proposed that the term encompasses a range of processes, including working memory, inhibitory control, the initiation and monitoring of actions, mental flexibility or set-shifting, planning, sustained attention, vigilance, and a range of other putative mechanisms. At times, the term 'executive function' has been used interchangeably with 'cognitive control', however there do appear to be important differences in their conceptualisation. Braver and Barch (2002), define 'cognitive control' as encompassing multiple additional cognitive domains in addition to EF, including episodic memory, working memory, prospective memory, inhibition and attention (p.809). Cognitive control is a more abstract concept, with a broader definition that describes the ability of the cognitive system to adjust itself to adapt to the performance of specific tasks (Botvinick et al., 2001). Executive function, however, is a more tightly defined construct. A number of models of executive functions exist (see Chan, 2008 and Purdy, 2011 for reviews of models of EF). Diamond (2013) conceptualised EF as having three primary components: inhibitory control, working memory and cognitive flexibility. This conceptualisation has been modelled on Miyake et al.'s seminal paper (2000) on executive functions. This tripartite model is commonly used when assessing executive function, as there are many cognitive tasks that purportedly measure these components. Below, each of the components is outlined in more detail, and a number of the most frequently used tasks are listed.

Inhibitory control is defined as the ability to control one's actions, attention, thoughts and emotions in the face of temptations, lures or strong internal predispositions (Diamond, 2013). It can be conceptualised as the ability to resist impulses, both internally and externally generated. For example, looking at inhibitory attentional control, it is the active control of what we pay attention to, known as 'top-down' (Theeuwes, 2010) attentional control. We can control which stimuli we can attend to or ignore, in line with our motivations or goals. Similarly, we can choose to inhibit or pay attention to cognitive stimuli such as thoughts or memories (Anderson & Levy, 2009). Examples of well-known tasks used to measure inhibitory control include the Flanker task (Eriksen &

Eriksen 1974), the Simon task (Hommel, 2011), the Sustained Attention to Response Task (SART, Robertson et al., 1997) and other go/no-go tasks (Cragg & Nation, 2008).

The second core component of executive function in this model is Working Memory (WM). WM involves the ability to hold and manipulate information that is no longer present (Baddeley & Hitch, 1994). WM is often characterized by its content, with the distinction made between verbal WM and visuospatial WM. Being able to hold information 'online' and manipulate it is essential for many cognitive tasks, such as language comprehension, mental mathematics, converting instructions into a plan of action and updating plans in the light of new information, re-ordering items on a list, and any other task that requires "holding in mind what happened earlier and relating that to what comes later" (Diamond, 2013, p.141). Common WM tasks include complex span tasks (e.g. backward digit-span, counting span, reading span), Corsi-Blocks task (Lezak, 2004), and n-Back tasks (Owen et al. 2005, Verhaeghen & Basak 2005); although it has been acknowledged that complex span tasks and n-Back tasks also involve other supposed cognitive functions, such as selective and sustained attention.

The third component of EF is deemed to be cognitive flexibility, which is defined as the ability to change perspectives. It is held that cognitive flexibility necessarily builds on inhibitory control and WM in that one must 'inhibit' the old perspective, and activate the new one using WM (Diamond, 2013). Examples are changing spatial perspective, changing thoughts about something, adjusting to changing demands. Other terms related to and often equated with cognitive flexibility include 'task-switching', 'set-shifting' and creativity. Common tasks used to measure cognitive flexibility include fluency tasks (verbal fluency, category fluency), and the Wisconsin Card Sorting Task (WCST; Milner 1963; Stuss et al. 2000). It has been recognised however that the WCST necessarily encompasses several components of executive functioning, including not only cognitive flexibility and 'set-shifting', but also response inhibition and abstract reasoning, hypothesis generation and problem solving (Hanks et al., 1999; Mukhopadhyay et al., 2007).

While the tripartite model of executive functions has been conceptually useful as a clearly demarcated account of cognitive processes against which researchers have been able to test hypotheses and measure outcomes of interventions, it is not clear that there exist experimental tasks that can measure isolated components of EF. This is because the 'core' components rarely work in isolation, either in response to laboratory challenges or in everyday real-life situations. Research has historically linked EFs to the frontal lobes (Alvarez and Emory, 2006), as many studies of patients with frontal-lobe lesions

show deficits in EFs (e.g. Milner, 1963). Milner (1963) introduced the WCST as a measure of prefrontal dysfunction, and this led to many studies linking WCST performance to frontal lobe damage (e.g. Nelson, 1976; Robinson, Heaton, Lehman & Stilson, 1980). As neuroimaging studies exploring neural activation during the WCST have shown widespread activation across both frontal and non-frontal regions in healthy controls, the current consensus is that the WCST cannot distinguish between frontal and non-frontal brain regions (see review by Nyhus & Barcelo, 2009). Similarly, brain imaging research has also shown that other common tasks purporting to measure working memory, inhibitory control and cognitive flexibility most frequently engage broadly distributed brain regions (Uttal, 2013; Niendem et al., 2012). Indeed, the most pervasive feature of the brain activation associated with some of the most common tests of executive function (e.g. the n-Back task, the Trail Making Task, the Flanker Task) is engagement of the classical motor networks (Cremen & Carson, 2017; Uttal, 2013). Uttal (2013) has boldly stated that in fact the most robust conclusion that can be drawn from neuroimaging data pertaining to cognitive processes is that "it's not doing what it's supposed to do" (p.363)- namely, to locate modular cognitive processes in a particular brain region(s). Thus, the traditional cognitive science view of the brain and executive function is not supported.

1.3.3 Evidence for an enactive model of executive function

A radical departure from this traditional view of executive function is an alternative definition that is grounded in action. In line with the enactive view of cognitive science, Koziol, Budding and Chidekel, (2011) posited that the primary purpose of EFs is to control behaviours and, as such, our continuous interaction with the environment. Under this perspective, EFs have been defined as the tasks an organism uses to act independently for the purpose of its survival (Koziol et al., 2011; Miller, 2007). It is still the predominant view in cognitive neuroscience that the frontal cortex is the seat of executive functions (Koziol et al., 2014), echoing the dualistic separation of mind and body. However, below I will outline research has shown both that (a) brain regions traditionally thought to be primarily involved in 'motor' functions are associated with EFs, and (b) that motor learning and action execution involves 'cognitive' processes.

It is becoming increasingly evident that sub-cortical brain regions classically considered to be 'motor' areas are involved in executive functioning, such as the cerebellum (Houk et al., 2007; Ito, 1993; Koziol et al., 2011; Schmahmann, 1997) and

basal ganglia (Isoda & Hikosaka, 2011; Miller, 2007). Seminal reviews of neurobiological data have shown that there is little evidence for the traditional 'perception-cognition-action' model of cognition, and that classical motor networks are involved in many 'cognitive' tasks (Cisek & Kalaska, 2010; Shadlen & Movshon, 1999; Singer, 2001). Experimental studies have highlighted the importance of the motor system in decision-making (Wyss, König & Verschure, 2004), visual perception (Flanagan & Johansson, 2003), working memory (Moreau, 2013), attention (Schuch et al., 2010), spatial cognition (Moreau, 2012), and language (Block et al., 2008). For example, studies examining the neural correlates of decision-making have found that in sensorimotor brain regions, namely those responsible for guiding online movement execution, that there is overlapping activation in regions encoding decision variables and the motor-response attributes (Gold & Shadlen, 2007). Thus, movement planning is related to decision-making processes that have long been thought to be 'higher-order' cognitive processes (Cisek and Kalaska, 2005, 2010). A recent large-scale Activation Likelihood Estimation (ALE) meta-analytic study examining approximately 6,000 participants across 346 fMRI experiments of inhibition or reasoning revealed that EFs are mediated by not only cortical structures, but by subcortical regions including the putamen and the thalamus (Ardila, Bernal & Rosselli, 2017).

In addition, it has been shown that motor learning is not confined to areas traditionally conceptualised as 'lower' motor regions of the brain (e.g. cerebellum and basal ganglia). One of the hallmarks of motor control is the capacity to inhibit actions, an ability which appears to decline with age. Levin and colleagues (2014) reviewed literature that used transcranial magnetic stimulation (TMS) to elucidate the links between declining motor function in healthy older adults and changes in inhibitory functioning, proposing that this reduced capacity could originate at the interface between prefrontal and premotor cortices and M1. Hinder and colleagues (2012) have previously proposed that amongst older adults, motor task performance is linked to the ability to modulate inhibition, through specific neurotransmitter systems (GABAA and GABAB mediated). Seidler and colleagues (2010) have suggested that motor control becomes increasingly dependent on central cognitive control mechanisms with age, and studies have demonstrated an increased recruitment of the prefrontal and sensorimotor cortices for performance of motor tasks with age (Hamacher et al., 2015; Heuninckx et al., 2005, 2008; Papegaaij et al., 2014). Heuninckx and colleagues (2008) carried out fMRI on older adults learning a complex motor coordination task. Performance was correlated with brain activation in not only classical motor regions, but also higher-level

sensorimotor regions and frontal regions involved in cognitive control. Thus, it is evident that 'inhibitory control' processes are not restricted to 'cognitive' tasks, but are essential for control of movement, especially as one gets older.

Along with inhibitory control process, other executive functions have been suggested to be related to motor capabilities. Working memory (WM) processes, a subcomponent of executive function, are involved in movement planning and movement execution. When planning movements, WM processes hold goal-relevant information active so it can be transformed into movement programs (Ohbayashi, Ohki and Miyashita, 2003). Speigal, Kosender and Schack (2013) conducted an experiment to further examine this relationship, finding that movement execution and movement planning recruit distinct sub-domains of WM. Movement execution disrupts spatial memory, and movement planning was associated with both visual and verbal working memory. Developmental studies have shown that motor control and working memory are related from early in life (Gottwald et al., 2016). Trewartha and colleagues (2014) have shown that amongst older adults, poorer explicit memory is linked to reduced motor-learning capabilities and impaired motor learning. Again, it is evident that motor control and executive functions, such as WM, that are classically considered to be 'higher-order' cognitive processes, have commonly been falsely dichotomised in the study of the brain and cognition. Elsewhere, Taubert, Lohmann, Marguiles et al. (2011) found that after just one week in which participants learned a complex balancing task, they saw increased frontoparietal network connectivity, and after six weeks individual differences on task performance modulated this change in connectivity.

Unfortunately, the false dichotomy between the concepts of motor and cognitive functions has limited the scope of interventions attempting to enhance cognitive functions in older adults. Nonetheless, action-based interventions to enhance cognitive function are becoming increasingly popular of late. It is important to review and critically analyse these paradigms in order to maximally exploit the potential of physical training programmes.

1.4 Seeking to Improve Executive Function in Older Adults

Following the enactive turn in cognitive science and Anderson's neural reuse theory, the "motor chauvinist" would contend that the exploitation of a person's ability to control their actions and interact with and adapt to the external environment should be central to interventions whose aim is to enhance cognitive function. Interventions that

have used physical activity (PA) to improve cognitive functions have shown promise in this regard, especially regarding benefits in executive function. PA interventions use exercise and movement programmes to improve physical capability, with the expectation that there will also be a positive impact in the cognitive domain (Bamidis et al., 2014). Some researchers have suggested that physical activity is the lifestyle factor that has shown the most promise with regard to enhancing cognitive function in older adults (e.g. Bherer, Erickson & Liu-Ambrose, 2013; Hertzog et al., 2008; Kramer et al., 2004). Indeed, PA interventions, in the forms of aerobic or cardiovascular training, appear to yield somewhat more consistent positive effects upon executive function in older adults than 'cognitive training' approaches which have targeted specific sub-domains of executive function (Colcombe & Kramer, 2003; Smith et al., 2010).

Overall, however, the exact pattern of benefits bestowed by physical activity on cognitive function remains ambiguous. Meta-analyses tell conflicting stories, with some finding no effects of aerobic exercise on any cognitive functions (Young, Angevaren, Rusted & Tabet, 2015), and others finding improvements on all cognitive measures used (Northey, Cherbuin, Pumpa, Smee & Rattray, 2017). Most, however, have found some positive effects and some null effects. Positive effects have been found in relation to executive function (Colcombe & Kramer, 2003; Smith et al., 2011), working memory (Roig, Nordbrandt, Geertsen & Nielsen, 2013); processing speed (Smith et al., 2011; Angevaren, Aufdenkampe, Verhaar, Aleman & Vanhees, 2008); and attention (Angevaren et al., 2008; Smith et al., 2011). However, it is important to note that these same meta-analyses found null results for working memory (Smith et al., 2011; Angavaren et al., 2008); memory (Roig et al., 2013; Angevaren et al., 2008), and processing speed (Colcombe & Kramer, 2003). Thus, conclusive evidence demonstrating 'wide' transfer, i.e. showing benefits for untrained cognitive skills, has yet to be shown in either the PA or the Cognitive Training domain (Diamond & Ling, 2016).

Potential reasons for the inconclusive results concerning PA interventions abound. There is huge methodological variation in study protocols, including, but not limited to, the type of exercise used, the dose and intensity of the intervention, the cognitive outcome measures used, the different study populations, and the control group characteristics (Etnier et al., 1997; Voelcker-Rehage & Nieman, 2011). Cross-sectional research has shown that older adults who are more active and who have higher levels of aerobic fitness exhibit better executive function performance (Boucard et al., 2012; Colcombe & Kramer, 2003; Voelcker-Rehage et al., 2011), so maybe the time-frame of

interventions are simply inadequate, and years of activity is what is necessary in order to reap the cognitive benefits.

The mechanisms underlying the putative benefits of physical activity interventions are still unclear. Different theories have proposed that the key mediators are variously: cardiovascular health (Kennedy et al., 2016); the social interaction that comes from exercise (Anderson, Winett, Wojcik & Williams, 2010); increased production of hormone and growth factors such as brain-derived neurotrophic factor (BDNF) (Kennedy et al., 2016); or insulin growth factor-1 (IGF-1) (shown in rodent models, Cotman & Berchtold, 2002). The main body of research that has looked at the relationship between PA and cognitive functions has used interventions that have primarily focussed on increasing cardiorespiratory or 'aerobic' fitness, that is they measure improvements on the PA training by assessing changes in participant's maximal oxygen uptake (VO_2 max) (e.g. Angevaren et al., 2008). The assumption that aerobic activity alone is necessary to reap the cognitive benefits has been frequently challenged (e.g. Etnier et al., 2006; Forte et al., 2013; Diamond & Ling, 2016). Etnier and colleagues (2006) carried out a meta-regression of aerobic interventions and found that whilst there was a reliable positive association between participation in Physical Activity and cognitive function, this advantage was not predicted by individual changes in levels of 'aerobic' fitness, i.e. increases in VO_2 max.

It has been suggested that physical activity interventions that do not include a 'cognitive' element fail to produce benefits for executive functions (Diamond & Ling, 2016). For example, in literature exploring the effects of PA on executive function in children, repeated calls have been made for attention to be paid to the 'cognitive' components of physical activity (e.g. Best, 2010; Pesce, 2012; Sibley and Etnier, 2003; Tomporowski et al., 2008, 2015). The characterisation of complex actions here as 'cognitive' is potentially problematic and reminiscent of dichotomous thinking about the mind and body, with the frontal cortex as the 'control centre' that thinks, reasons and governs actions. However, the general idea that interventions characterised by challenging motor control demands (for example, in relation to the requirements for movement planning, multisensory integration and the reformulation of muscle synergies) bears serious consideration. One study comparing aerobic exercise that did not involve the use of complex movement strategies (e.g. treadmill running, rowing machines, spinning bikes) to a 'cognitively demanding' physical activity (a 'designed sport' based on freestyle wrestling), and to cognitive training alone reported no benefit for aerobic exercise alone (Moreau et al., 2015). In contrast, individuals who were engaged in the

motor fitness intervention (designed sport), which involved a high degree of 'motor' learning and emphasised movement planning and the precise coordination of actions, exhibited the greatest improvements in cognitive measures. Similarly, Oswald and colleagues (2006) compared cognitive outcomes from older adults who were randomly assigned to physical training (which emphasised balance, perceptual and motor coordination and flexibility), cognitive training, combined physical and cognitive training, psychoeducational training (a training series on overcoming everyday problems), combined psychoeducational training and physical training to a non-active control. Five years post-intervention, they found the strongest preservation of cognitive function for those in the combined physical and cognitive training group. Thus, it is evident that multiple components are involved in physical activity interventions, in addition to aerobic capacity, such as complex motor planning, balance, flexibility, perceptual and motor coordination, and other processes involved in motor control. It is now being recognised that these components may be the principal contributors to the cognitive benefits seen after physical activity interventions (Northey et al., 2017). However, there is a paucity of research exploring the non-aerobic components involved in training interventions (Pesce, 2012) which could potentially moderate or enhance cognitive gains (Yan & Zhou, 2009). In the wake of inconclusive results regarding aerobic physical activity, and as the boundaries between variants of ''cognitive'' and ''physical'' training become blurred, it is imperative that methodologies are refined in order to clarify which elements of physical activity are important in this relationship.

1.4.1 Motor Fitness

Classes of physical activity that place greater explicit emphasis upon the generation of coordinated movement and allude to a concept of 'motor fitness' are now receiving particular attention (e.g. Voelcker-Rehage et al., 2011; Berryman et al. 2014; Forte et al, 2013; Moreau et al., 2015; Pesce et al., 2013; Johan et al., 2016). Motor fitness has been conceptualised by Voelcker-Rehage and colleagues as encompassing components such as flexibility, speed, balance and fine coordination (2010). It alludes to training that emphasizes the generation of coordinated movement, distinct from cardiovascular capacity and muscle strength. Motor fitness is also held to reflect efficiency in the engagement of processes traditionally conceived of as 'higher-order cognitive', such as attention and working memory, that are fundamental for mapping sensation to action, anticipatory planning, and the adaptive components of postural control and coordination (Voelcker Rehage et al., 2010).

Associations have been seen between motor fitness measures and general cognitive function in older adults. Cross-sectional data indicate that elements of 'motor fitness' in older adults, such as movement speed, balance and fine motor coordination, are strongly associated with levels of executive functioning (Voelcker-Rehage et al., 2010; Holtzer et al., 2006, 2012). For example, subtasks of the Timed Up and Go, which is a measure of mobility (Podsiadlo & Richardson, 1991), have been associated with levels of cognitive impairment (Mirelman et al., 2014) and poor cognitive function (Robertson, Savva and Kenny, 2013) and the prediction of future cognitive decline in older adults (Auyeung, Lee, Kwok and Woo, 2011). Elsewhere, in a cross-sectional study looking at the relationship between both cardiovascular and motor fitness and cognitive function in 72 older adults (62-79 years), motor fitness was assessed using 7 different tasks (Voelcker-Rehage et al., 2010). These tasks measured flexibility (a shoulder flexibility task), speed of movement (hand and feet tapping tasks), agility, balance (backwards beam walk and a one-leg-stand), and dexterity (the Purdue Pegboard test). They found a strong positive correlation between motor fitness and cognitive function in older adults.

It has also been shown that motor fitness is related to structural differences in the brain. For example, one cross-sectional study looking at the relationship between motor fitness and cognitive function (Baezner et al., 2008) measured gait and balance, using the Short Physical Performance Battery. This comprised three tasks including stands and chair stands to measure balance, and a 4-meter walking test to assess gait. A composite score was calculated (0-12) giving equal weight to these three tasks. Gait speed was also measured on an 8-metre course, and single leg stand (up to 30s) was measured. Baezner and colleagues found that gait and balance deficiencies were related to age-related white matter changes, explicitly showing that coordination training can lead to structural brain changes. A later intervention study carried out by Niemann, Godde and Voelcker-Rehage (2014) found that 12 months of coordination training, emphasising balance, movement speed and fine motor coordination, was related to changes in hippocampal volume in older adults. This is significant as it has been shown that hippocampal volume is associated with cognitive health in ageing (Petersen et al., 2000; Kramer et al., 2007)

1.4.2 Interventions to Improve Motor Fitness

Based on evidence indicating that motor fitness can cause structural changes in the brain, and that motor fitness is related to improved executive functioning in older adults, researchers have recently explored the use of motor fitness training in attempts to

enhance cognitive function. Motor fitness training interventions emphasise multisensory integration, strategic planning of movements, and mapping sensation to action. They use training that is highly variable, using combinations of movements that need to adapt to changing task demands (e.g. Voelcker-Rehage and Nieman, 2013). There has been a number of efforts to design novel interventions that emphasise motor fitness and share some characteristics with popular sports or measurement tasks to ensure they are 'ecologically valid', i.e. that experimental settings are likely to be similar to real-world naturalistic settings (Tupper and Cicerone, 1990). One example is the "Designed Sport" intervention used by David Moreau and colleagues (2015), which consists of a training programme based on freestyle wrestling training. It has been suggested by its proponents that there are certain characteristics of training that force the participant to think about their movements in a strategic manner. For example, additional problem-solving demands are imposed at various intervals during the training. One such addition, referred to as 'perceptive problem solving', involves the degradation of the participant's visual feedback by blindfolding them or by putting them in specific positions, such as back-to-back. A second imposition, named 'motor-problems', consists of training on "novel, non-automatic motor sequences via unfamiliar situations" (p.46), by presenting progressively more complex motor coordination requirements. Finally, they add in 'cognitive problem-solving' where participants are required to respond to auditory stimuli (sound and number) by producing an increasingly complex series of movements. By combining the benefits of physical training with additional 'cognitive' demands, the authors sought to optimise both cognitive and physical outcomes. The results reflected these intentions, and participants involved in the designed sport intervention showed the greatest improvements on measures of cognitive function in comparison to an aerobic exercise group and a WM training group.

Ben-Soussan and colleagues (2013) similarly designed an intervention that emphasised elements of movement that they hypothesised might lead to greater transfer from the motor to the cognitive domain. They focussed on creativity as their outcome variable of interest, as measured by the 'Alternate Uses Task' (AUT). In their 'Quadrato-Motor Training' (QMT), developed by Paoletti (2008), young adults (ages 20-35) begun the training by standing in the corner of a marked-out box (0.5m squared). Upon hearing a verbal instruction, they were required to make one-step movements to one of the three other corners of the square. The aim of the QMT was to increase "attention, coordination and creativity" (p2). They compared this to a group carrying out 'Simple Motor Training' (SMT), which had similar motor demands but lower cognitive demands, and a group

doing ‘verbal training’ (VT), which had similar cognitive demands but lower motor demands. In the SMT, participants consistently moved from corner 1-2-3-4, and in VT, participants responded to the verbal instructions by stating where they would move given a particular instruction, but they remained stationary in one corner. Training was a single session lasting seven minutes. They found that scores of ideational flexibility significantly increased only for participants who received QMT, and that reaction time scores improved for both movement conditions (QMT and SMT) but not VT. The authors suggest that the complexity of the movement involved in the QMT was the driver of the beneficial effects on creativity in the QMT group. Interestingly, EEG measures taken showed performance on ideational flexibility was correlated with changes in bilateral frontal alpha coherence, with only the QMT group showing improved alpha coherence. Greater complexity, such as a greater number of directions for movement and a whole-body response requirement, were given as the reasons for this effect. This was supported by previous work showing that greater alpha coherence accompanied more complex finger movements (Manganotti et al., 1998).

In another study of the effects of the QMT training (seven-minute session) on spatial cognition and reflectivity (Ben-Soussan et al., 2014a), QMT was found to significantly improve test performance on the Hidden Figures Test (Glicksohn & Kinberg, 2009) in comparison to SMT and VT. Longer-term interventions involving QMT have been carried out by Ben-Soussan and colleagues (2014b), who found that after a month of daily QMT practice, better performance was observed on a speeded reading task amongst both dyslexic and non-dyslexic readers. Similar improvements in alpha coherence were observed in the non-dyslexic controls (however, this was not observed in dyslexic participants). More recently, it was shown that 3 months of daily QMT led to enhanced intra- and inter-hemispheric connectivity (Ben-Soussan et al., 2015; 2017).

Voelcker-Rehage, Godde and Staudinger (2011) carried out a coordination training intervention that consisted of a whole-body focused programme aimed at improving both fine and gross motor-coordination using complex movements to improve a variety of skills. These included ‘balance, eye-hand coordination, leg-arm coordination, spatial orientation and reaction to moving objects/persons’ (p.4). The training was carried out using an assortment of fitness equipment such as balls, skipping ropes, bands, boards, to carry out a variety of activities. Training took place over 12 months, 3 times a week for 1 hour, and participants missing over 25% of training were excluded from analysis. They assessed motor fitness using three tasks. ‘Action speed’ was measured using a foot

tapping task (Voelcker-Rehage and Wiertz, 2003, as cited in Voelcker-Rehage, Godde & Staudinger, 2011) where seated participants were timed tapping both feet simultaneously on a marker for 20 seconds. Secondly, 'reaction speed' was measured using a 'stick-fall test' (Ehrler and Huth, 2000), which measured the ability to catch a falling stick, using falling distance as the outcome measure. Balance was again measured with the one-leg-stand, where participants are required to balance on one leg for up to 20s. Coordination training was found to have a beneficial effect on both accuracy and reaction time performance on the Flanker task (Eriksen and Eriksen, 1974) and the Visual Search Task (Hommel, et al., 2004), reflecting improvements in executive function and visual-spatial processing. Similar benefits were seen for participants who carried out cardiovascular training, but not for those taking part in the active control intervention, which consisted of relaxation and stretching.

Another study assessing motor training was carried out by Berryman and colleagues (2014), who compared executive function performance of healthy older adults in three intervention groups: lower body strength training plus high-intensity cardiovascular training, upper body strength training plus high-intensity cardiovascular training, and gross motor activities (GMA) training. Training took place over 2 months, consisting of three 60-minute sessions per week. Training for all groups consisted of a 10-minute warm-up and 50 minutes of cardio/strength/GMA training. GMA training consisted of two weeks of stretching activities, followed by three weeks of additional locomotion activities, described as walking about obstacles and carrying objects to a goal destination. For the final three weeks, ball manipulation tasks were added in (i.e. juggling, targeted throwing). Cognitive challenge was incorporated into the training by emphasising response inhibition and cognitive flexibility, for example by changing the order of learned task-sequences and switching tasks between different learned stimulus-response associations. Results showed that executive function, measured with the random number generation task, improved significantly and equivalently across all three conditions; however, no active control group was included, so practice effects cannot be ruled out as a cause of this improvement, although it has been reported that the RNG is not susceptible to practice effects (e.g. Audiffren et al., 2009). The authors conclude that multiple pathways could lead to benefits for cognitive function in older adults.

Forte and colleagues (2013) carried out an intervention comparing the benefits of 'multicomponent' training to resistance training for cognitive function in older adults (aged 65-75). Participants trained twice weekly (60 minute sessions) for 3 months on either multicomponent training or resistance training. Multicomponent training (MCT)

consisted of 15 minutes warm-up and 30 minutes of 'conditioning', which focused on improving balance/ coordination/ strength/ agility, and 30 minutes of mat-based exercises (stretching, strengthening, relaxation). Exercises required participants to walk/ skip/ jog through space while using their arms for various tasks, such as to catch or throw objects. Difficulty was manipulated by changing the speed, and using obstacles that participants had to interact with (e.g. step over/ avoid). MCT was designed to emphasise "coordination, balance, agility, and cognitive executive control" (p.19). Both interventions led to significantly improved performance on tasks measuring inhibitory capacity (measured by the Random Number Generation task). Again, the emphasis in this intervention was on a variety of movements and reproducing environmental challenges facing older adults in everyday life (Forte et al., 2013) as outlined by Shumway-Cook and colleagues (2002).

More recently, Johann et al., (2016) compared the outcomes of a cardiovascular intervention to a 'motor-cognitive coordination training' intervention amongst sedentary and active young participants (mean age 23.4). Motor coordination training consisted of 5 minutes of juggling exercise as a warm-up, followed by two (out of a choice of three) 20-minute exercises based on the 'Lifekinetic' training regime (Lutz, 2012, as cited in Jonann, 2016). Exercise 1 consisted of jumping in a 2x2 grid to a predefined sequence, with both arm movement tasks and cognitive tasks being added in to increase difficulty (e.g. throwing and catching a ball or repeating number sequences). In Exercise 2, participants hit a tennis ball from hand to hand using 2 tennis rackets, and upon hearing a verbal instruction, had to try and hit one of ten pylons arranged in a surrounding semi-circle. Again, task difficulty was increased with additional movement instructions (such as moving feet in a pre-defined pattern) or concurrent cognitive instructions (e.g. if specific categories of animals were called out, a specific pylon had to be hit). In Exercise 3, participants were required to move to one of 30 'bonnets' of a certain colour that were laid out on the floor, all the while carrying out simultaneous ball-catching tasks of varying difficulty. Performance on all three exercises improved by the end of the training period (totalling 8 hours over 6 weeks). Amongst physically active participants, no transfer was seen from coordination training or cardiovascular training to the cognitive domain. A significant reduction was seen in interference costs on inhibitory control measures (Flanker task) in the coordination group, whereas these effects were not exhibited by a cardiovascular training group and control group. However, this effect was only seen in the experiment looking at sedentary participants.

It seems that motor fitness training interventions have led to changes in performance on cognitive outcome measures in a range of different settings. We can interpret these results under the model of neural reuse introduced earlier (Anderson, 2016), which has stated that the same finite reserve of neural resources are used and reused in multiple ways as needed. The evolution of "higher-order" cognitive processes has been promoted by the utilisation of existing neural resources and behavioural strategies, not specific 'targeted' adaptations. It is probable that neural adaptations exhibited in response to the demands of the complex motor training tasks were centred on the common neuronal architecture subserving tasks conceived as both 'motor' and 'cognitive'. In essence, complex motor training emphasises action planning and execution in response to environmental demands and it follows that these interventions could also lead to changes in tasks measuring 'cognitive' function.

1.4.3 Methodological Issues in Interventions Attempting to Enhance Cognitive Function

In order to fully explicate the relationship between motor training and cognitive gains, a number of methodological issues in the study of cognitive enhancement must first be addressed. In much of the current research aiming to explore how cognitive function can be enhanced in older adults through a physical intervention, it is popular to utilise or adapt a pre-existing genre of activity (such as aerobic or cardiovascular training, dance, yoga, tai chi, wrestling etc.) for deployment as a training intervention. This methodology has many benefits concerning the ecological validity of the intervention; it means that these interventions are things that people enjoy participating in. However, this methodology does have its pitfalls. One problem with this approach is that there is enormous variability across interventions, even within those that aim to train participants in the same activity (e.g. treadmill running, high-intensity interval training). In addition, despite efforts to control intervention protocols, it is necessarily the case that different participants tend to have quite different experiences. It is hard to measure the dose of training given to individuals in such interventions, and thus the challenges of relating any enhancement of cognitive function to specific elements of the training regime are formidable. Moreover, given the many degrees of freedom with respect to which movements may be varied in achieving task goals (Bernstein, 1967), it is extremely challenging to identify the causal agents that mediate the benefits of such interventions.

In addition, many of these activities were designed with the general goal of leisure; they have to be enjoyable otherwise they would not attract a following. Health

benefits may also be a common aim in some of the more modern iterations (e.g. Zumba/ aerobics classes/gym-based interventions). This gives rise to the additional challenge of parsing the role played by such factors as motivation in giving rise to positive outcomes. In short, there are many features of these activities that challenge the application of the analytic and interpretative models used conventionally in experimental science. It is unsurprising, given these limitations, that there is huge variability in the results reported in physical and motor intervention studies. The variation encompasses not only the basic question of whether a positive or null outcome is obtained; it also extends across the range of measures of cognitive function that are typically employed.

In addition, there are many limitations that are common across interventions, irrespective of whether these are based upon physical or cognitive training. These include a lack of active control groups (e.g. Forte et al., 2013). It is well known that without adequate control groups, there are no grounds to suggest that changes in cognitive function were caused by the training intervention. However, in the study of older adults, particularly important for a number of reasons are the use of 'active' control groups. 'Active' means that they do train on some task, and do not simply take the pre-test and post-test outcome measures. Firstly, longitudinal studies have shown that social engagement is associated with improved cognitive functioning in older adults (e.g. Scarmeas, Levy, Tang, Manly & Stern, 2001; Wang, Karp , Winblad & Fratiglioni, 2002). Moreover, participants in the active control task must have equivalent expectations of improvement to the control group, otherwise psychological phenomena, such as motivation or expectation, may influence outcomes (Boot, Simons, Stothart & Stutts, 2013; Simons et al., 2016). In other words, only by equating every task parameter except the factor of interest is it possible to infer that differential outcomes among the training group are attributable to that factor (Simons et al., 2016).

Further, adequate measures of cognitive function are essential in correctly measuring the outcomes of interventions aiming to enhance cognitive function. Firstly, an appropriate number of tasks are needed to enable adequate scope of measurement; as indeed there may be widespread benefits of training beyond the intended domain. It may be that the effects of an intervention are missed because the outcome measure used does not reflect the changed capacity, or might not be sensitive enough to measure changes over the time-frame of the experiment. It is advisable to use a number of tasks to try and capture the essence of the cognitive gains. In addition, using multiple tasks purportedly measuring the same outcome allows for stronger claims of transfer post-intervention if all such tasks show reliable differences (Moreau, Kirk & Waldie, 2016).

Moreover, many interventions fail to show causality in the relationship between trained task and changes in cognitive performance, due to difficulties measuring the adaptation to the intervention (e.g. Etnier et al., 2006; Moreau et al., 2015). This lack of explanatory power needs to be addressed by exploring individual responses to training and consequent (individual) changes in cognitive outcomes. Often the number of people carrying out an intervention makes it prohibitive to track specific motor adaptations at an individual level. Thus, there is a lack of insight into the characteristics of movement that might contribute to positive cognitive outcomes, such as movement speed, precision and the specific patterns of muscle activity engaged. There are boundless 'degrees of freedom' in the complex movements that are trained in many interventions, making changes in specific elements hard to parse out. Looking at the wide range of 'motor' or 'coordination' or 'whole-body' training programmes that have been employed in the literature, it is evident that there is little uniformity amongst the training tasks used. They vary in intensity, dose, and training activities undertaken; but what is clear is that there is more often than not an emphasis on variety and complexity in these tasks. Whilst it has been argued that this complexity is an essential component for cognitive benefits to be observed (e.g Moreau et al., 2014), inferences in relation to the mechanisms underlying these benefits are precluded by the fact that the interventions may not only lead to changes that were directly intended as a consequence of the experiment, but simultaneously along several dimensions. In order to explore this question, and to seek to investigate in the most rigorous manner whether motor training can cause improvements in cognitive function, it is necessary to carry out tightly controlled interventions. Ideally these should have the characteristics mentioned above, namely that they include an 'active' control group that are engaged in an adaptive task, that is equivalent in demands in every sense with the exception of the motor behaviour being examined. In addition, individual dose and response to training should be tightly controlled. One pragmatic solution to the methodological issues raised above is the adoption of specific 'motor learning' paradigms, that allow us to tightly control key elements of the task, such as task complexity, the dose of training that individuals get, and measurement of the key movement characteristics that lead to transfer to the cognitive domain.

1.4.4 Using motor learning paradigms to inform interventions

Certain paradigms have proved to be particularly successful in providing a platform upon which to establish the neurophysiological basis of motor learning. Naturally, it is these paradigms that have also been employed to examine the facets of cognition that play a role in motor learning (e.g. Anguera et al., 2010; Seidler, Bo & Anguera, 2011), and to study the degree to the relevant neurophysiological processes are altered through the course of ageing. What is currently lacking in the field of cognitive enhancement in older adults is a direct application of the motor learning principles thus derived, particularly when exploration of the beneficial effects of motor/coordination training on cognitive function in older adults is the matter at hand.

The execution of a motor task is achieved by activating muscles, and recruiting assemblies of muscles together in what are known as muscle 'synergies' (Bernstein, 1967). All movement is necessarily also constrained by the properties of the neuromuscular-skeletal system (Carson & Riek, 2001). It has been shown that practice on a motor task leads to modification of the patterns of muscle synergies that are used, within the limits imposed by the neuromuscular-skeletal system (Carson & Riek, 2001). Practice on a motor task typically leads to improved performance, such as shorter time taken to perform the task, fewer errors in the movement outcome, or less effort needed to carry out the movement (Layet al. 2002; Shemmell et al., 2005a). Adaptation to a motor task is dependent on the goals of the task. For example, if the goal of a task is to hit a target as quickly as possible, then adaptation to the task might comprise strategies for accomplishing this goal such as greater movement speed or less path deviation, leading to faster target acquisition. Accordingly, refinement of a motor skill leads to changes in performance variables associated with the goals of the task (Shemmell et al., 2005b).

Thus, although we may not always be conscious of the processes involved in refinement of a motor skill, there are nonetheless complex interactions between muscle synergies and the central nervous system that work in synchrony to optimise motor performance. Learning a new motor skill, or 'sensorimotor adaptation', involves not only the creation of cerebellar 'internal models' (neural models that are said to encode visuospatial information) (Wolpert and Ghahramani, 2000), but also working memory and attentional processes (Taylor and Thoroughman, 2007, 2008; Anguera et al., 2010). Learning a new motor skill has been shown to involve brain regions that encompass areas traditionally thought of as 'cognitive', for example the 'early' stages of skill learning,

where improvements are observed over a short number of trials, have been shown to be associated with the DLPFC and dorsal anterior cingulate cortex (Anguera, Russell, Noll & Seidler, 2007; Anguera, Reuter-Lorenz, Willingham & Seidler, 2011; Taylor & Ivry, 2014). It has been shown that sensorimotor adaptation to a novel visual environment (such as a rotated environment) is dependent on 'spatial' WM processes, and further that variations in individual adaptation to such environments can be predicted by activity in the DLPFC (Anguera et al., 2011). It has been suggested previously that spatial WM is used when learning new action sequences, to 'chunk' individual components of action together, and to process motor error information, which can be subsequently used to update actions (Seidler, Bo & Anguera, 2012). 'Later' learning stages, thought to occur over hours or days of practice (Karni et al., 1998), have been thought to be more heavily dependent on cerebellar or parietal brain regions (Flament et al., 1996; Seidler & Noll, 2008).

Hence, training on a motor task that requires the precise formulation of muscle synergies and spatial planning is thought to engage 'higher-order' cognitive regions, and thus will potentially lead to improved performance on cognitive measures. Training on sessions over a number of days will engage both the 'slow' and 'fast' learning processes associated with skill acquisition and refinement. In addition, motor learning paradigms allow us to parse out changes in key performance variables, such as movement velocity or deviation from the direct path to a target, that lead to improved performance. Based on the limitations outlined above in attempts to associate improved training performance on complex whole-body training programmes with changes in cognitive performance, the issue of whether measures of improvement on key performance variables have an association with enhanced performance on cognitive outcome measures following a motor training intervention need to be explored. In recognition of this need, the case advanced here is that sensorimotor learning paradigms provide tasks that have been shown previously to engage widespread activation in the brain, and have been associated with executive function performance, such as spatial working memory tasks (Anguera et al., 2011). Moreover, they allow for the precise measurement of the underlying movement characteristics that contribute to performance enhancements.

1.5 Summary of Key Concepts

- Traditional cognitive science models of cognition that conceptualise cognition in a "perception-cognition-action" framework have led to attempts to enhance cognitive function that have focused on training localised functions and subdomains of cognition (e.g. Jaeggi et al., 2008; Anguera et al., 2013). These training programmes have for the most part failed to show 'wide' transfer to untrained tasks (e.g. Lampit et al., 2014; Melby-Lervag et al., 2016; Owen et al., 2010; Simons et al., 2016; Souders et al., 2017).
- Alternative ontologies of the brain and cognition have led to action-oriented frameworks that emphasise the importance of motor functions in the evolution of "higher-order" cognition (Engel et al., 2013; Koziol et al., 2011). Anderson's theory of Neural re-use (Anderson, 2014) posits that the same finite reserve of neural resources are used and reused in multiple ways as needed.
- A key implication of Anderson's theory of neural reuse is that rather than having to be supported by a targeted adaptation, a more parsimonious account of "higher-order" cognitive processes is that they utilise existing neural resources and behavioural strategies.
- In support of this 'enactive' view of cognition, with the advent of neuroimaging technologies, much evidence has shown that rather than occupy localised brain regions, 'cognitive' and 'motor' functions are associated with widespread activation patterns in the brain (Uttal., 2013).
- There is increasing evidence suggesting that physical activity interventions can lead to enhanced cognitive performance in older adults (e.g. Colcombe & Kramer, 2003). Recent research has demonstrated that motor-fitness interventions have shown promise in enhancing executive functions in older adults (e.g Voelcker-Rehage et al., 2011; Moreau et al., 2015). However, the enormous heterogeneity in studies and within individual response to training tasks make this relationship hard to explicate.
- Motor learning paradigms should be exploited in order to test the hypothesis that motor-training can lead to enhanced cognitive performance in older adults. This will allow for the tight experimental control of dose and measurement of movement characteristics that potentially mediate this relationship.

1.6 The Current Study

The premise that underpinned the current study is that the changes in brain function induced by motor-coordination training extend beyond the classical motor network, to encompass regions that play a critical role in cognition. Therefore, by training on a motor-coordination task, benefits may be seen in performance on cognitive tasks. Using motor learning paradigms to impose tight control of experimental variables, and to measure changes in performance, we sought to establish whether motor coordination training can enhance executive function in older adults.

***Hypothesis*:** Motor-coordination training interventions designed to accentuate multisensory integration, spatial planning and the precise formulation of muscle synergies, will improve performance on measures of executive function in older adults to a greater degree than a control group that are not engaged in a motor training task.

Chapter 2 Can training on a coordinated wrist movement task lead to improved cognitive function in older adults?

2.1 Introduction

The body of evidence indicating that motor-training interventions may contribute to improvements in executive function has been growing in the past decade (e.g. Voelcker-Rehage et al., 2011; Berryman et al. 2014; Forte et al, 2013; Moreau et al., 2015; Pesce et al., 2013). Despite this, there remain methodological concerns that limit the degree to which causal attributions can be made. The generality of the supposed effects, and in particular the scope ("near" or "far") of the transfer from the motor to the cognitive domain also remains to be determined.

Prominent among the methodological demands that remain to be satisfied is the requirement that interventions permit tight control and monitoring of the dose of (motor) training that individuals receive. Similarly, it is desirable that the complexity of the training task – which should be defined precisely in terms of motor control requirements, is amenable to systematic manipulation. More specifically, it is a corollary of the hypotheses that have been advanced herein, that the extent of transfer from the motor to the cognitive domain scales with the level of demand imposed by the training regime upon neural circuits that (also) play a central role in the mediation of executive function.

The class of rapid aimed arm movement tasks, that have been used for more than a century to examine various facets of motor control and learning, exhibit characteristics that appear to satisfy many of these requirements. Furthermore, these tasks have long been utilised to explore older adults' fine motor control (and indeed cognitive function) (e.g. Darling, Cooke, & Brown, 1989; Yan, 2000; Yan, Thomas, & Stelmach, 1998). It is generally assumed that in aiming to a visually specified target location, a pre-programmed motor plan controls the initiation and initial guidance of the movement (Larish & Stelmach, 1982; Schmidt, Zelaznik, & Frank, 1978). We produce movement by activating muscles, and assemblies of muscles, together in the context of muscle 'synergies' (Bernstein, 1967). Movements are also constrained by the structural properties of the neuromuscular-skeletal system (de Rugy et al., 2009; Shemmell et al., 2006). Upon initial exposure to a new task, there is a general tendency for existing muscle synergies to be deployed. Through repetition, or directed practice, existing synergies are

refined, and new synergies are composed, in a manner that promotes performance of the task. In other words, practice on a motor task leads to modification of the patterns of muscle synergies used, and gives rise to improved efficiency of motor commands that optimise the recruitment of such synergies (Carson & Riek, 2001). Depending on the nature of the task, improved performance may be expressed as a reduction in time to completion, as a reduction in the number of "errors" (e.g. misdirected movements that fail to make contact with an object), or in the effort needed to carry out the movement (Lay et al. 2002; Shemmell et al., 2005a). Necessarily, therefore, the nature of the adaptations that occur in the course of learning are contingent both on the intrinsic nature of the motor act, and specific to the goals of the task at hand. For example, if the goal of a task is to hit a target as quickly as possible, the adaptations may comprise an increase in muscle torque – expressed as higher peak velocity of movement, and/or the generation of movement trajectories that deviate to a lesser degree from a direct path to the target. Thus, refinement of a motor skill leads to changes in performance variables associated with the goals of the task (Shemmell et al., 2005b). Depending on the speed and goal of the task, "online" adjustments mediated by sensory feedback may then be used to modify the unfolding movement trajectory (Burton, 1987; van Donkelaar & Franks, 1991). The customary view is that the effective contribution of feedback mediated control decreases with the rapidity of the aiming movement. Adaptations that occur in the course of learning may also be expressed via changes in the efficiency and effectiveness with which feedback mediated control is implemented. From the model outlined above, it is clear that the processes involved in performance on such motor tasks are complex and require the precise coordination and execution of many functions within the brain and central nervous system. These are recruited in both the planning and initiation of the movement and in the online movement corrections based on the visual feedback. It is on this basis that we propose that training on such tasks engage not just classical motor regions, but widespread brain areas, including regions often classified as "higher-order" regions such as the prefrontal cortices. Thus, the adoption of these training tasks in attempts to enhance cognitive function is an experimental strategy that warrants investigation.

In order to make inferences about the nature of the mechanisms underlying transfer from motor training to the cognitive domain, careful experimental design is necessary. This is especially pertinent in the domain of cognitive enhancement, where a number of methodological concerns have been all too frequently ignored in past studies. Particularly important in the domain of cognitive enhancement in older adults is the use

of active control groups that receive the same amount of social contact as the training group, as it has been shown in longitudinal studies that that higher levels of social engagement are associated with better cognitive function in older adults (Scarmeas, Levy, Tang, Manly & Stern, 2001; Wang, Karp , Winblad & Fratiglioni, 2002). Indeed, it is now recognised that a number of confounds are introduced if the training groups and control groups are treated differently (Shipstead, Redick & Engle, 2012). In order to adequately infer that outcomes are not due to placebo effects or other psychological phenomena (e.g. motivation), the active control group must have the same expectation of improvement to the training group (Boot, Simons, Stothart & Stutts, 2013). Thus it is essential that the experience of both groups is of participation in a training intervention (Rosnow & Rosenthal, 1997). To ensure that this is the case, ideally both groups should be engaged in adaptive tasks that change over the course of the training period: one involving the component of primary interest (e.g. motor training), and the other imposing equivalent demands with respect to all dimensions other than the one that constitutes the essence of the intervention. In the event that this objective can be achieved, a basis is thus provided to attribute any effects of the intervention to the component of primary interest. As an aside, imbuing active control participants with expectations that they will get better at the adaptive task over the course of training should not raise ethical concerns, as if an adaptive task is used, participants should expect that they might improve over the course of the intervention. However, it should not be suggested that the active control task will lead to enhanced cognitive function in any way (nor should it be for the training group). It is clearly also desirable that study designs adhere to best practice with respect to such characteristics as the blinding of investigators to group allocation, and that procedures are in place to ensure the random assignment of participants to groups.

The choice of task(s) used to examine potential transfer of training related adaptations to the cognitive domain is of critical importance, as this also determines the weight of the inferences that can be drawn. In view of this dependency, it has been recommended that multiple measures should be used to minimize measurement error and provide reliable and accurate estimates of the target construct (e.g., Shipstead et al., 2012; Moreau et al., 2016). Ideally, tests that span a range of cognitive domains or executive functions should be used, in order that all aspects of transfer are likely to be captured (Morea, Kirk and Waldie, 2016). In addition, the assessment tools should be sufficiently sensitive in their facility to capture any changes that may arise as a consequence of an intervention. It is widely acknowledged that practice effects can lead to erroneous attributions of improvement. This is a particular concern in the case of serial assessments

of cognitive function on the basis of standardised tests (e.g. Goldberg et al., 2015). It is essential, therefore, that assessments of cognitive function utilise tests that permit different variants to be employed prior to and following the intervention.

2.1.1 The Current Study

The aim of the current study was to extend 'proof of concept' concerning the putative association between motor-coordination training and changes in cognitive function. In order to address this aim, we conducted a blinded randomised controlled trial (RCT) that employed a motor training intervention that permitted the complexity of the task and the dose of training to be manipulated. We controlled for placebo effects by ensuring that both the training and control groups had equivalent expectations of improvement, by ensuring that participants were unaware that they were in a control group and by providing an adaptive control task to ensure motivational factors did not influence results. We aimed to control for the misinterpretation of practice effects on the cognitive tasks by utilising different task variants of the cognitive tasks at the pre, post and intervention test sessions, and by ensuring that the control group that followed the same pre- and post-intervention testing procedures. In addition, we minimised the effects of experimenter influence by blinding the researcher carrying out the cognitive tasks to the participant group allocation.

Participants in the training group carried out training on a coordinated wrist movement task, whereas participants in the control group trained on an active control task. The motor training task employed herein consisted of a target-acquisition task requiring coordinated wrist movements to acquire targets located on a screen (Figure 2.1.1-2 below). Eight different target positions were possible, and or their acquisition they required the appropriate selection and activation of distinct muscle synergies. Participants could not improve performance by simply enhancing the preparation of a single movement (and muscle synergy). Rather, upon presentation of the target, the CNS had to first select and compose the synergy appropriate for a movement to that target location. This required integration of the initial visual presentation of the target, followed by selection of the appropriate action, a process thought to rely on the basal ganglia (Gurney, Prescott & Redgrave, 2001). In addition, it has been shown that with practice, the CNS 'simplifies' the task by reducing the number of muscle synergies involved in carrying out actions, thus reducing the necessity of commands needed for muscle activation (Shemmell et al., 2005a).

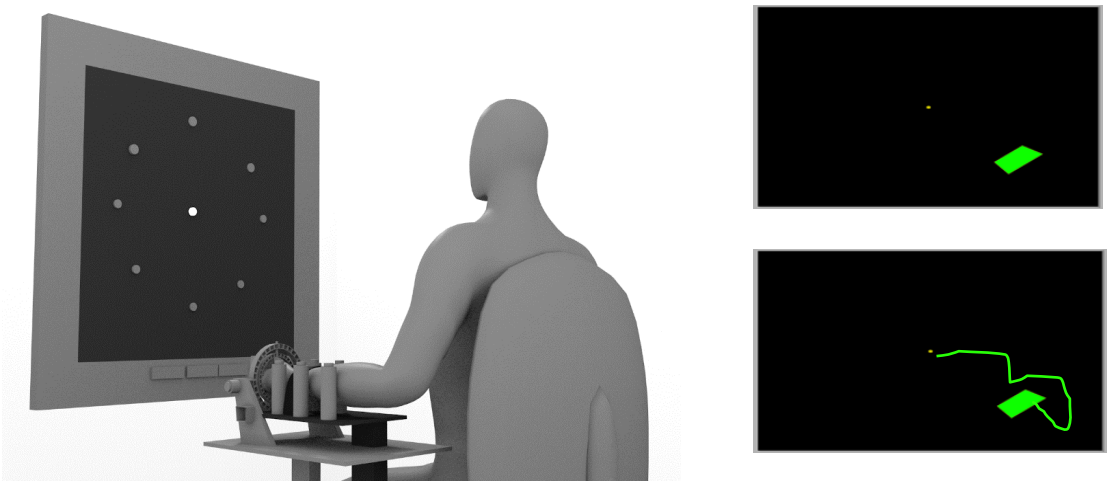

Figure 2.1.1-2.1-1 Participants in the training group were required to hit targets appearing on a screen using coordinated wrist movements. Targets were located in eight locations around a central home position (left). Participants could use online visual feedback modify their movement trajectory (right).

Over the course of training, in addition to refinement of the composition of the required muscle synergies, there was also the potential to enhance the effectiveness with which sensory feedback (including the online visual feedback provided by virtue of the structure of the task) was used to modify movement trajectories following their initiation (Figure 2.1.1-2, above). The provision of concurrent visual feedback during movement execution permits online error detection and correction. In order to exploit sensory feedback to alter existing muscles synergies in order to improve performance, the brain/CNS needed to precisely calibrate the visuomotor mapping of the environment and transform the visual information into the suitable motor commands (Hinder et al., 2010). These elements of the task were thought to be critical in providing the potential for positive transfer to the cognitive domain.

Individual responses to the intervention – in terms of the extent of motor learning, were quantified on the basis of performance variables (which captured both movement outcomes and characteristics of the kinematics). Cognitive function was assessed using a carefully selected suite of tests, using variants that are robust to practice effects.

Participants in the active control group were required to carry out a similar task, but one that did not require any movements. In the same experimental set-up, targets appeared onscreen in front of the participants. Eight different target positions were

possible. Participants had to pay attention to the visual stimuli and count targets appearing onscreen that were blue in colour. A random number of blue targets would appear onscreen in every trial. Participants had to remember the number, and report it back to the experimenter at the end of each block, but were not required to make any movements to 'acquire' the targets. Target size got smaller over the course of the training period to increase task difficulty.

The premise that underpinned the current study is that the changes in brain function induced by motor-coordination training extend beyond the classical motor network, to encompass regions that play a critical role in cognition. We deployed an intervention in which coordinated movements of the wrist joint were used to acquire targets presented in the context of a classic visual aiming task. The motor demands of the task were increased progressively over the course of five days of training by decreasing the size of the targets. Performance on a standardised version of the task was assessed prior to the training period, and three days and ten days following the cessation of training. Tests of cognitive function were administered contemporaneously.

***Hypothesis*:** A motor-coordination training intervention designed to accentuate multisensory integration, spatial planning and the precise formulation of muscle synergies, will improve cognitive function in older adults to a greater degree than an active control intervention.

2.2 Materials and Methods

2.2.1 Participants

Forty-six healthy community-dwelling older adults were recruited using ageing research databases, local community groups and online volunteer boards. Three participants dropped out before completion (two due to illness, and one due to a scheduling conflict), leaving 43 participants in total.

Participants underwent telephone screening prior to enrolment in the study, to exclude anyone with evidence of neurodegenerative disease. Participants were pre-screened using a telephone adaptation of the MMSE (Newkirk et al., 2004) and a health screening questionnaire. Two further participants were excluded from data analysis as they were left-handed. The remaining 41 participants were right-handed, as assessed using the Edinburgh Handedness Inventory (Oldfield, 1971; mean Laterality Quotient: +88.3). Participants were aged over 65 (65-90 years, Mean=71.2, SD=5.4, 10 Males). All participation was voluntary, and all participants provided written informed consent to the procedures, which were approved by the Trinity College Dublin School of Psychology Ethics Committee and conducted in accordance with the Declaration of Helsinki.

2.2.2 Trial Protocol

A blinded randomised controlled trial was carried out over the course of four weeks. Participants were randomly assigned to one of two conditions: motor training (n=21) or active control (n=20). Groups did not differ significantly in terms of age ($t(52)=0.37$, $p=0.711$) or gender (X-squared = 1.2781, $df = 1$, $p= 0.258$). Both groups attended initial 'pre-test' sessions, where a host of cognitive and motor assessments were carried out (outlined below). Subsequently, they completed five 30-minute training sessions on 5 consecutive days (Monday – Friday) at the university. Following training, they again completed the battery of cognitive and motor tasks at a post-test session soon after training (3/4 days) and a Retention session following a subsequent period of time (8-10 days) (see figure 2.2.2-1 for an outline of the experimental protocol). Both participants and researchers were blinded in this experiment. Participants were randomly allocated to one of two groups (training or control). The participants were not aware that there was an alternative training condition. Group allocation was determined using a computer-generated random number sequence prepared by an investigator who was not

involved in recruitment, intervention or data collection. Different researchers were involved in (a) carrying out pre-test, post-test and retention test sessions ("assessors") and (b) carrying out the intervention training sessions ("trainers") (figure 2.2.2.1). The person carrying out the pre/post/retention assessments was naive as to the allocation of each participant to training condition.

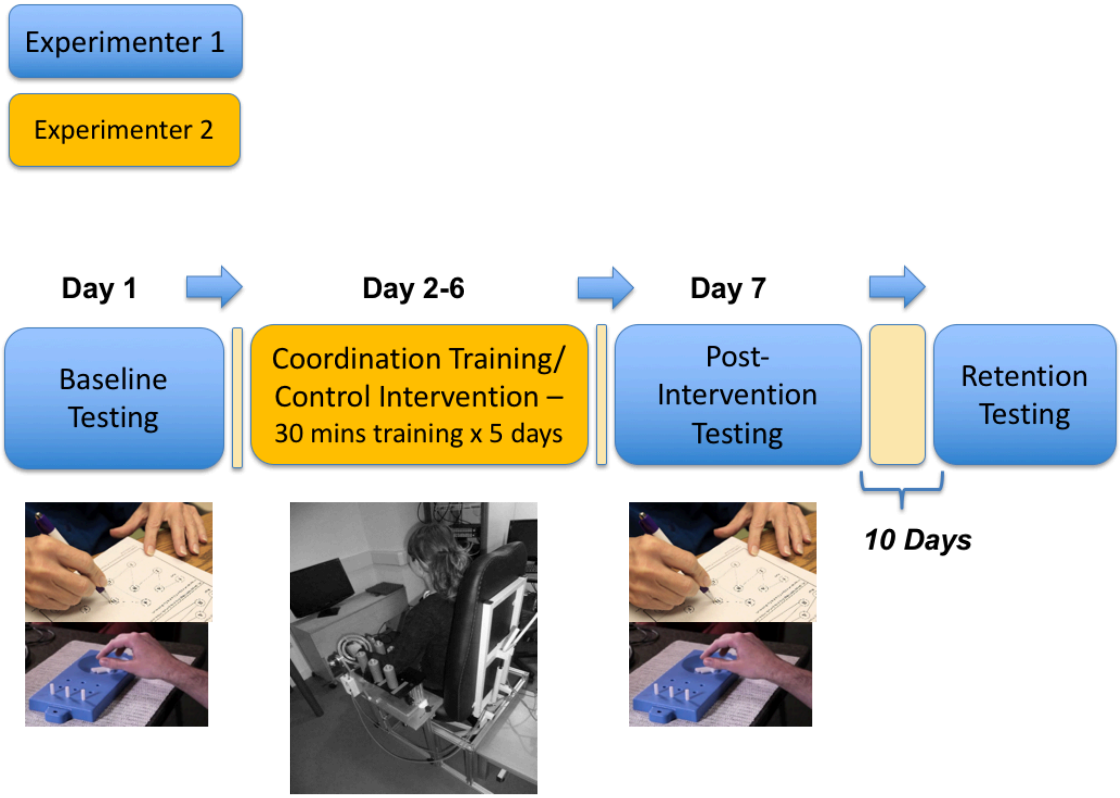

Figure 2.2.2-1 Schematic illustration of the experimental protocol. Assessors carried out the pre-test, post-test and retention-test sessions, and were blinded to the intervention condition of participants.

2.2.2.1 The motor training intervention

On each of 5 training days (Monday-Friday), training group participants each had to carry out 4 blocks of a motor task using their left limb only. The motor intervention comprised training on a centre-out target acquisition task. Participants had to acquire visual targets appearing on a screen in front of them using coordinated wrist movements (see Figure 2.2.2-3 below).

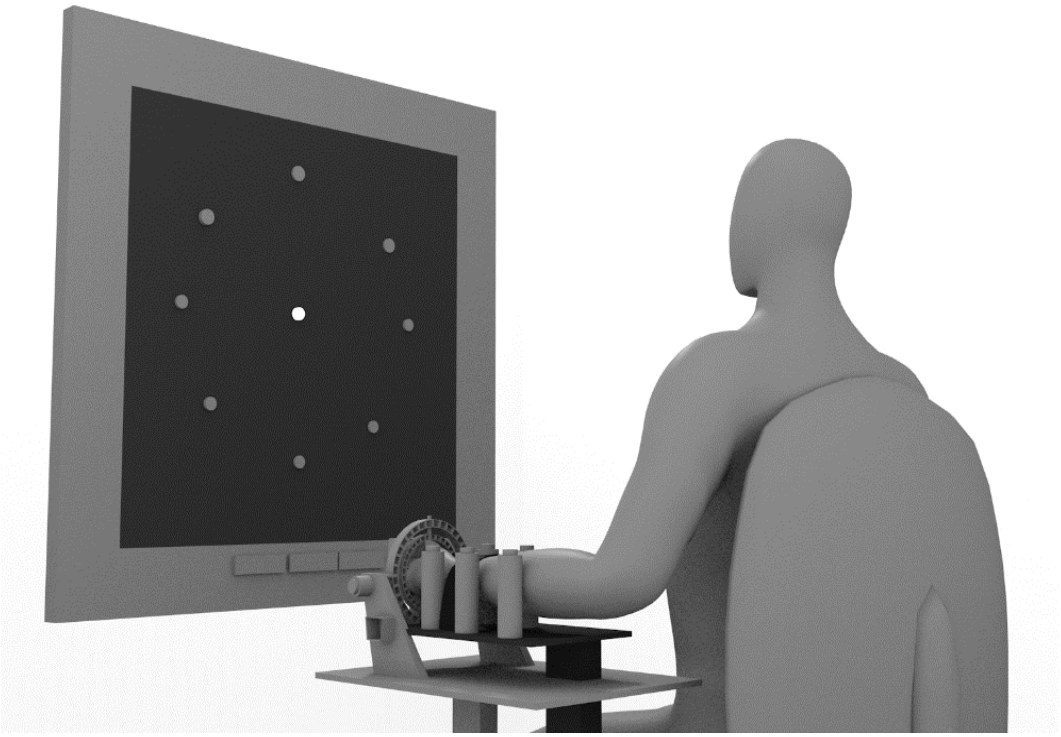

Figure 2.2.2-3 Experimental set-up. Participants were seated .75m from a visual display (not to scale), with their forearm secured in place to prevent lateral motion. Participants were strapped onto the manipulandum which controlled the position of the cursor onscreen. Participants in the training group were required to hit targets appearing on a screen using coordinated wrist movements They were required to move their wrist in 2 degrees of freedom (flexion-extension and ulnar-radial deviation, or combinations of these movements) in order to hit one of eight targets appearing onscreen. Targets were located in eight locations around a central home position. Participants could use online visual feedback modify their movement trajectory (right).

Participants were comfortably seated in an adjustable experimental chair positioned 0.75 m in front of a 24" computer screen, with the centre of the screen at eye level (figure 2.2.2-4. Their upper limbs were supported on horizontal platforms, with lateral motion prevented by foam-covered posts placed on either side of each arm. The head, neck, torso and feet were also fully supported. The forearms were stabilised in mid-pronation and the elbows semi-flexed (100-120˚). Each hand was securely fixed within a manipulandum (Figure 2.2.2-4, panel (a)) that was instrumented to transduce

displacements of the wrist in two degrees of freedom (i.e. flexion-extension, and radial-ulnar deviation). The outputs from the transducers were low-pass (analog) filtered at 8Hz, and then sampled at 2000Hz. The transduced displacement of the wrist was projected onto the LED screen as a yellow cursor in the shape of a circle. The cursor responded to displacement of the wrist in an intuitive way such that extension of the right wrist, and flexion of the left wrist, would move the cursor to the right. For both limbs, radial deviation moved the cursor upwards, and so on.

A circular "home position" was presented in the centre of the screen. The participant was instructed to move the cursor into this central circle in order to begin each trial. Holding the cursor in the central circle for 50ms caused a target to appear. Targets located at 45° intervals around the circumference of a circle defined by a radius corresponding to 15° of wrist displacement (8 distinct positions) were presented in pseudo-random order. For example, acquisition of target position 3 required that 15° of radial deviation be produced in combination with 15° wrist flexion. The participant was instructed that following the presentation of a target, they should move the cursor to the target "as quickly and as accurately as possible". There was continuous (i.e. concurrent) visual feedback of cursor position, and participants could use this online visual feedback to correct their movement trajectory as they moved towards the target. If the cursor reached the target region (10% of distance from the origin to the centre of the target), and was then maintained continuously within this region for 50ms, a tone (60ms, 900-Hz sinusoid) signalled successful target acquisition. At this time both the cursor and the target were extinguished. In the event that a target was not acquired within a period of 4 seconds following its presentation, the target was extinguished and the screen refreshed. The participant was asked to relax following each trial - in order to return the cursor to the home zone (i.e. the wrist in a neutral position). The next target appeared 2–3 s later. Custom Labview (National Instruments, Austin, TX) programmes were used to implement all procedures for stimulus presentation and data collection.

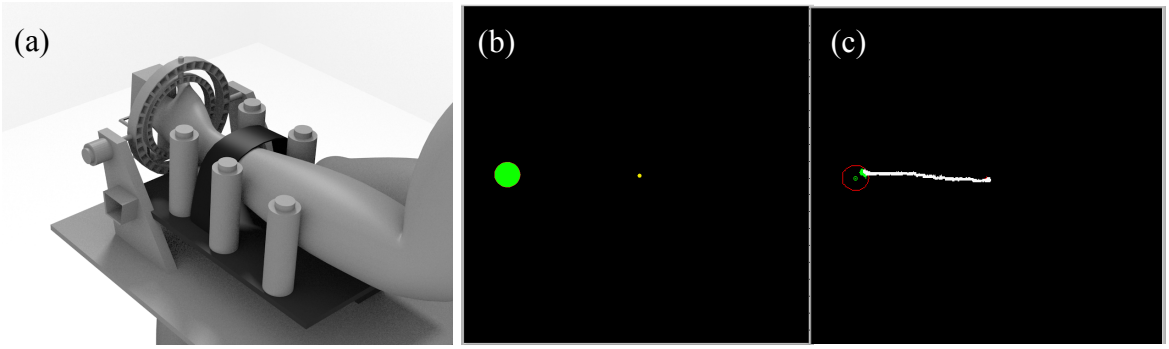

Figure 2.2.2-4 (a) A 2 Degree-of-Freedom Manipulandum was used to record wrist flexion & extension. The hand was positioned in the horizontal plane, with the fingers straightened in line with the palm. After holding the limb in 'neutral' position in the home position in the centre of the screen, a target would appear at one of 8 locations on the screen (b). Participants received no online visual feedback of their cursor position during movement, however they received post-trial visual feedback of their cursor trajectory (c).

In each session, there were 32 repetitions per block, totalling 4 blocks (therefore 32*4= 128 repetitions per session). Each block lasted 4 minutes, with a 1-minute break between blocks, thus the training sessions lasted approximately 20 minutes per day. Task difficulty was increased incrementally over the course of the training period by manipulating the target size. This became progressively smaller over the course of each session. The first target size used on the following day corresponded to the final target size presented on the previous day. Targets decreased in size in decrements of 1 mm per block over the course of 4 blocks per day (3.75 x 3.75 pixels on screen resolution of 96DPI) (Table 2.2-1).

Table 2.2-1 Progression of target size over the intervention period

Training Session	**Target Size in Degrees** *(corresponding diameter in mm)*			
Block	**1**	**2**	**3**	**4**
Day 1	10° (20mm)	9.5° (19mm)	9° (18mm)	8.5° (17mm)
Day 2	8.5° (17mm)	8° (16mm)	7.5° (15mm)	7° (14mm)
Day 3	7° (14mm)	6.5° (13mm)	6° (12mm)	5.5° (11mm)
Day 4	5.5° (11mm)	5° (10mm)	4.5° (9mm)	4° (8mm)
Day 5	4° (8mm)	3.5° (7mm)	3° (6mm)	2.5° (5mm)

2.2.2.2 Active Control Task

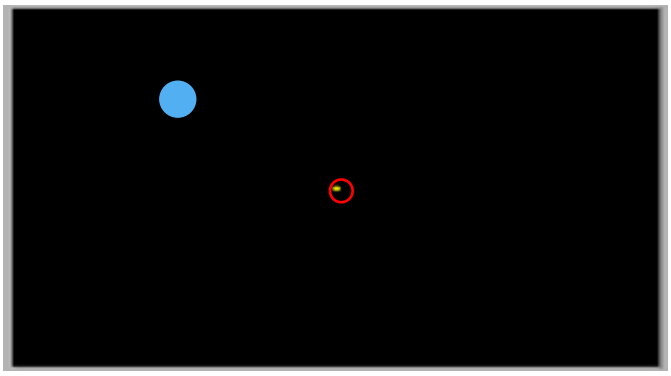

Figure 2.2.2-5 The active control task. The active control task closely resembled the visual display in the motor training task, however, participants were not required to make wrist movements to hit the target. They simply had to count how many blue targets appeared. Target size diminished as in the motor training task.

The control task schedule was identical to that of the motor training group, consisting of 4x4-minute blocks of training held on 5 consecutive days. The settings were also identical to that used for motor training, with participants sitting in the same chair and identical targets appearing onscreen - in order to keep attentional demands consistent across groups. However, limb movements were not required in the control task. Each of the 8 targets appeared four times (in pseudo-random order) in each block of 32 trials. The participants were asked to count the number of instances that a target was blue in colour (the frequency of blue target occurrence was varied randomly between 4-9 times per block, Figure 2.2.2-5). Participants were asked for the total after each block, and given verbal feedback on their performance with a view to keeping them engaged in the task. Over the course of the 5 training sessions, the size of the targets was decreased progressively during the course of each block, using the schedule described for the motor training condition. The target size progression was identical to that used in the motor training condition (Table 2.2-1). The intent was to increase task difficulty in precisely the manner of the motor training task.

2.2.2.3 Pre-, Post- and Retention Training Motor Assessments

Participants were comfortably seated in an adjustable experimental chair positioned 0.75 m in front of a 24" computer screen, with the centre of the screen at eye level (figure 2.2.2-3). Their upper limbs were supported on horizontal platforms, with lateral motion prevented by foam-covered posts placed on either side of each arm. The head, neck, torso and feet were also fully supported. The forearms were stabilised in mid-

pronation and the elbows semi-flexed (100-120˚). Each hand was securely fixed within a manipulandum (Figure 2.2.2-4, Panel a) that was instrumented to transduce displacements of the wrist in two degrees of freedom (i.e. flexion-extension, and radial-ulnar deviation). The outputs from the transducers were low-pass (analog) filtered at 8Hz, and then sampled at 2000Hz. The transduced displacement of the wrist was projected onto the LED screen as a yellow cursor in the shape of a circle. The cursor responded to displacement of the wrist in an intuitive way such that extension of the right wrist, and flexion of the left wrist, would move the cursor to the right. For both limbs, radial deviation moved the cursor upwards, and so on.

The pre- and post-training motor assessments comprised a centre-out target acquisition task. A circular "home position" was presented in the centre of the screen. The participant was instructed to move the cursor into this central circle in order to begin each trial. Holding the cursor in the central circle for 50ms caused a target to appear. Targets located at 45° intervals around the circumference of a circle defined by a radius corresponding to 15° of wrist displacement (8 distinct positions) were presented in pseudo-random order. For example, acquisition of target position 3 required that 15° of radial deviation be produced in combination with 15° wrist flexion. The participant was instructed that following the presentation of a target, they should move the cursor to the target "as quickly and as accurately as possible". There was continuous (i.e. concurrent) visual feedback of cursor position. If the cursor reached the target region (10% of distance from the origin to the centre of the target), and was then maintained continuously within this region for 50ms, a tone (60ms, 900-Hz sinusoid) signalled successful target acquisition. At this time both the cursor and the target were extinguished. In the event that a target was not acquired within a period of 4 seconds following its presentation, the target was extinguished and the screen refreshed. The participant was asked to relax following each trial - in order to return the cursor to the home zone (i.e. the wrist in a neutral position). The next target appeared 2–3 s later. Custom Labview (National Instruments, Austin, TX) programmes were used to implement all procedures for stimulus presentation and data collection.

The right (transfer) limb was always assessed before the left (training) limb, and target size was held constant throughout the assessment. Prior to the initial pre-training assessment, the participant undertook eight practice trials (one to each target position), first with the right limb and then with the left limb. In each of the subsequent assessments, each limb was employed in four blocks of 32 trials (128 trials in total for each limb). Within a block, each target appeared on four occasions. The duration of each block was

approximately four minutes. There was a rest period of approximately 1 minute between successive blocks. The total duration of each assessment session was about 40 minutes.

2.2.3 Assessments

In addition to assessment of performance on the baseline visuomotor task, all participants completed a battery of cognitive and physical function tests before (pre) and after (post) training, and again approximately 10 days after their post-training session (retention session) (Figure 2.2-2 below).

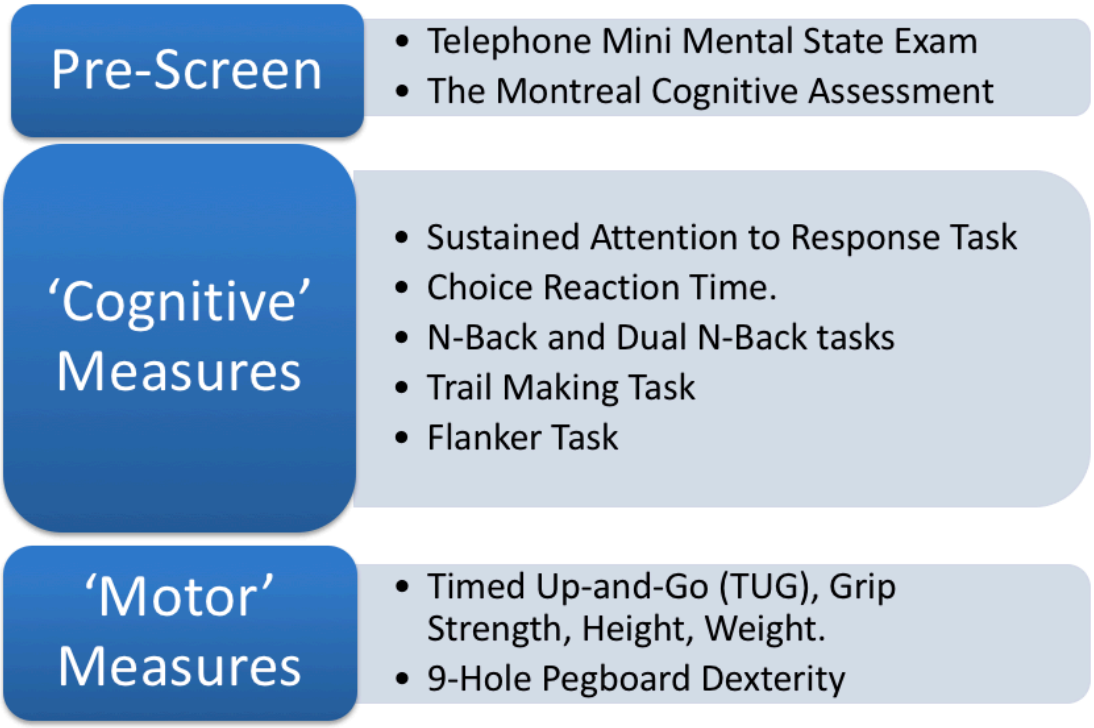

Figure 2.2-1 **A list of the measures used at pre-screen, and at the baseline, post-intervention and retention sessions.** Pre-screen measures were used before participants commenced on the cognitive and motor measures at the initial baseline session. The remaining cognitive and motor measures were repeated across testing sessions.

In the initial (pre) session, additional measures were carried out to measure mobility and cognitive impairment. The Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) was designed as a rapid screening instrument for mild cognitive dysfunction. Handedness was measured using the Edinburgh Handedness Inventory (Oldfield, 1971). The Timed Up and Go task (Podsiadlo & Richardson, 1991) was used to assess mobility. The participants were required to stand from a seated position, walk three metres to a line marked on the floor, turn around and walk back to the chair and sit

down again. The researcher obtained the time taken to complete the task using a stopwatch. Anthropometric measurements were also taken, consisting of participant height (cm) and weight (kg) measured using a Salter electronic scales. Body-mass index was calculated from these measures (kilogram/metres squared).

The remaining tasks were conducted in each of the three testing sessions. These consisted of the flanker task, the Choice Reaction Time task, the n-Back and Dual n-Back tasks, the Trail Making Task and the Sustained Attention to Response Task (Table 2.2-2 Below).

Table 2.2-2 Cognitive measures and the corresponding underlying executive function measured in the task.

Task	Executive Function Domain
Flanker Task	Inhibitory control/response inhibition
Choice Reaction Time Task (CRT)	Processing speed, reaction time
n-Back and Dual n-Back Task	Working memory
Trail Making Task (TMT)	Cognitive flexibility, task switching/ set-shifting; visual search; motor speed; processing speed.
Sustained Attention to Response Task (SART)	Sustained attention, inhibitory control/ response inhibition.

These tasks were selected to capture all of the domains of executive function described in the tripartite model of executive functions (Section 1.3.2); working memory (n-Back and dual n-Back), inhibitory control (the SART and the Flanker tasks) and cognitive flexibility (the Trail Making Task). In addition, an attempt was made to use tasks that were used in the Irish Longitudinal Study of Ageing (TILDA) so that there would be population norms against which to benchmark participant performance.[1] These tasks were the CRT, TMT and the SART. The Flanker Task was selected as it has been used commonly in the literature associating cognitive enhancement with physical

[1]Due to inconsistencies in how data was collected in the TILDA study, it was decided to no longer pursue the use of TILDA data for benchmarking cognitive function.

training (e.g. Voelcker-Rehage, Godde & Staudinger, 2011). Finally, the n-back task variants were selected on the basis that they are among the most commonly used working memory tasks to be utilised in interventions to enhance cognitive function (e.g. Jaeggi et al., 2009). All tasks were carried out in a consistent order across participants and sessions. In all cases, however, alternate versions of the tasks (e.g. randomised order of stimuli presentation and/or stimuli) were used across baseline/ post-intervention and retention sessions in attempt to minimise practice effects (Benedict & Zgaljardic, 1998).

2.2.4 Tests of Cognitive Function

A Sony Vaio 15-inch laptop was used to run the battery of cognitive tests. Computer-based tasks were programmed using E-Prime 2.0, PsychoPy, and PEBL (Psychology Experiment Builder Language, Mueller 2014). Responses were collected using a PST Serial Response Box, computer mouse and the laptop keyboard with modified buttons.

2.2.4.1 Flanker Task

The Flanker task (Eriksen & Eriksen, 1974) is a speeded response time task that explores the effect of 'flanker' distractor stimuli on target identification reaction time (RT). RT typically increases when the target stimulus is surrounded by 'incongruent' distractor stimuli—letters or shapes from the target set that require a different response. In this version of the Flanker task, stimuli were presented in black against a white background. Each stimulus consisted of a row of one or five stimuli. Participants were to respond to a central target arrow that pointed either left or right by pressing a corresponding button on a response box with their left or right index finger. In some trials, the central target arrow was surrounded by two arrows on both the left and the right side. The arrows on the sides (the 'flankers') were either pointing in the same direction as the central target arrow ('congruent' trials) or pointing in the opposite direction ('incongruent' trials). Additionally, in some trials, no stimuli flanked the central target arrow ('no-flanker' trials) and in others, the flankers were straight lines ('neutral' trials) (Figure 2.2.3 below). Participants were instructed to respond as quickly as possible while avoiding errors. They performed 10 practice trials followed by the experimental block (80 trials each). The presentation order of the stimuli was randomized within blocks.

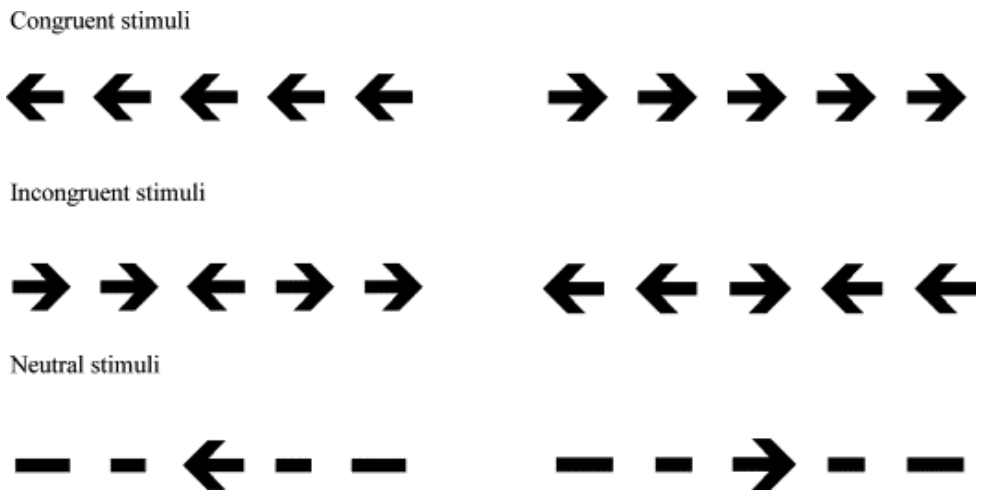

Figure 2.2-2 Flanker Stimuli: Congruent flanker stimuli pointed in the same direction as the central target arrow. Incongruent flanker stimuli pointed in the opposite direction to the central target arrow. Neutral flanker stimuli were straight lines without arrowheads.

In many studies, a direct comparison is made between responses in the presence of congruent flankers and responses in the presence of incongruent flankers. The interpretation of outcomes relies upon a ‘‘subtraction logic’’, whereby it is assumed that the same motor output is required in each instance, and that any difference between conditions (expressed via any given dependent measure) derives from other sources. With respect to the flanker task, the resulting contrast measure is hypothesised to be a ‘‘pure’’ measure of response inhibition, divorced of motor influence.

Outcome variables:

The flanker conflict cost was the primary outcome variable. The conflict cost was calculated as the difference in median RT performance between congruent and incongruent trials.

2.2.4.2 The Visuospatial n-Back Task and the Dual n-Back Task

The Visuospatial n-Back is a measure of working memory, although debate is ongoing as to its correlation with complex span tasks (e.g. Redick & Lindsey, 2013; Wilhelm, Hildebrandt, & Oberauer, 2013). The task used was identical to that of Jaeggi et al (2007, 2008, 2009). In this task, visual stimuli were presented on the computer screen. Visual stimuli consisted of blue squares that were presented on a black screen in one of eight equidistant locations around a constant central white fixation cross (figure 2.2-4). Participants were required to press a button if the visual stimulus matched that one presented *n* trials previously. The 1-back and 2-back conditions were used in this

trial. Stimuli were presented for 500ms, with an inter-stimulus-interval of 2500ms before presentation of the next stimulus.

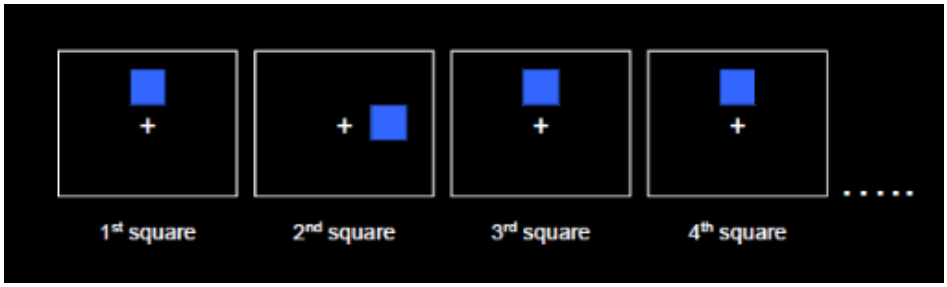

Figure 2.2-3 Visuospatial n-Back Task Stimuli: Visual stimuli in the form of blue squares appeared one after another in one of eight different locations around the computer screen. Participants had to remember the location of the square presented *n* trials previously.

The Dual n-Back was selected to assess executive functioning components, namely working memory (WM) capacity, in particular visuospatial memory and verbal memory, and also dual task processing (Jaeggi et al, 2003). There are thought to be task-specific differences between the Dual and regular n-Back tasks, such as increased demand on cognitive load and both visual and auditory elements, which may highlight age-specific deficiencies (Jaeggi et al., 2009). A computer-based version of the dual n-back was utilized, again using the 1-back and 2-back conditions. Participants were required to press one of two buttons on the PST response box; that were coloured either blue (visual stimuli) or red (auditory stimuli). As in the visuospatial n-back, the visual stimuli consisted of blue boxes presented in one of eight locations around a constant central white fixation cross. The auditory stimuli consisted of eight letters (C, D, G, K, P, Q, T, V) spoken in a clear female voice at the maximal laptop volume. Both visuospatial and auditory stimuli were presented simultaneously, and participants were instructed to press the blue (left) button, as before, if the visual stimuli matched the one presented n trials back, and to press the red (right) button if the auditory stimuli matching the one presented n trials before (see figure 2.2-5 below). If both stimuli matched those presented *n* trials back, participants were required to press both buttons. For non-targets, no response was required. Again, stimuli were presented for 500ms, followed by an ISI of 2500ms.

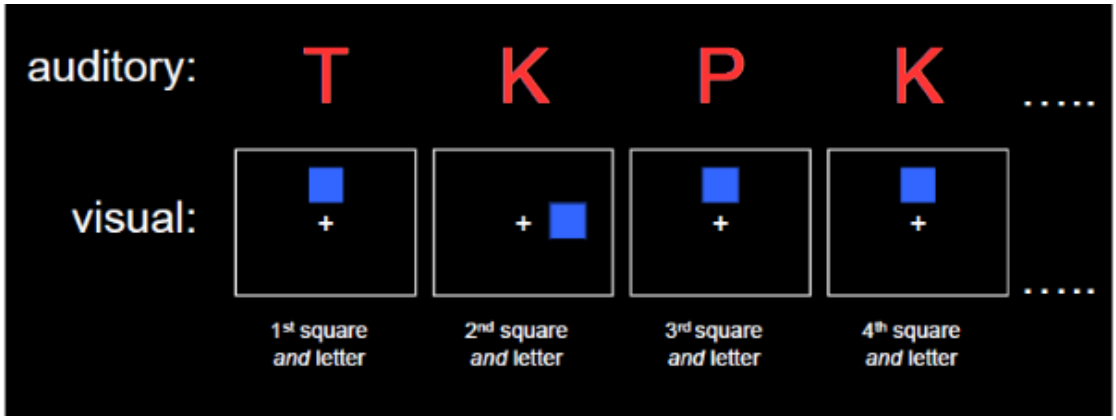

Figure 2.2-4 Dual n-Back Task Stimuli: Visual stimuli in the form of blue squares appeared one after another in one of eight different locations around the computer screen. Participants had to remember the location of the square presented *n* trials previously. Simultaneously, auditory stimuli were presented, in the form of letters of the alphabet. Participants had to remember the letter that was said *n* trials back.

Following visual instructions and a 20 practice trials of the 1-back condition, participants carried out 2-minute blocks (20 trials) of the 1-back condition, followed by a 2-minute block (20 trials) of the 2-back condition. Stimuli were presented in a pseudo-randomised order, with target position counter-balanced between blocks. All blocks contained 6 targets (30%) and 14 non-targets (70%). Participants were asked to respond as quickly and accurately as possible.

Outcome Variables:

For each level of the task (1-back and 2-back), the outcome variables were:

Accuracy: This was expressed as the proportion of Hits minus False Alarms (Snodgrass & Corwin, 1988).

Reaction Time: Median RT for hits only (however, as only 6 target responses are required throughout the task, the number of responses may be very low per block).

2.2.4.3 Trail Making Task Parts A & B

A computer-based version of the Trail Making Task was used to measure visual search and task switching capacities (Arbuthnott & Frank, 2000), motor speed and processing speed (Sanchez-Cubillo et al., 2009). Using a computer mouse, participants were required to connect 26 circles presented onscreen by clicking on them as fast as they could. There were two parts to the test; A and B. In part A, participants were required to connect the 26 circles in ascending numerical order (1-26). In the second condition, part B, they connected both numbers (1-13) and letters (A-M) in an alternating sequence of numbers and letters (e.g. 1-A-2-B-3-C-4-D… and so on, Figure 2.2-6 below).

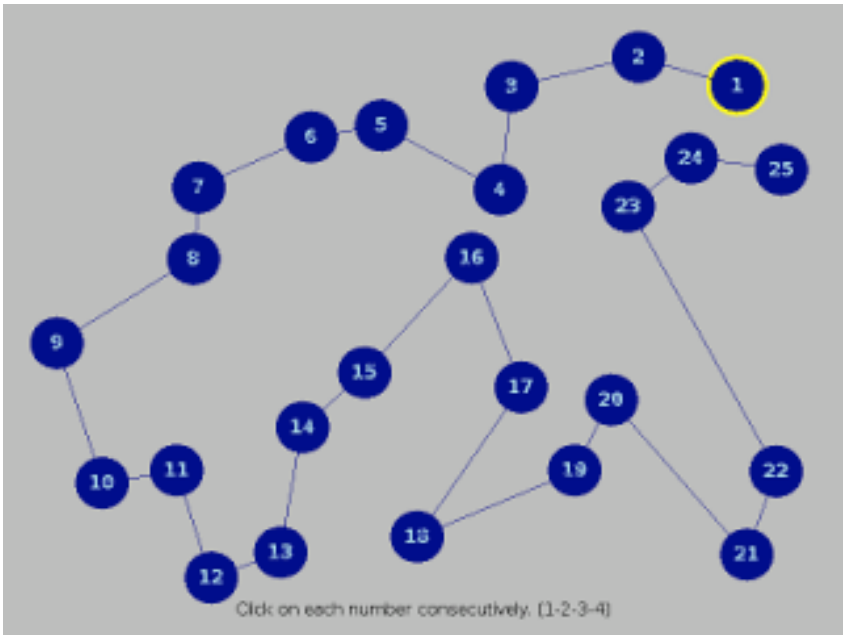

Figure 2.2-5 Screenshot of the completed Trail Making Task part A: participants are required to click on the circles in numerical order (1-26). When participants click on the correct circle, lines appear, connecting the circles.

Outcome Variables: The TMT B/A ratio score is used as a measure of executive function (Arbuthnott and Frank, 2000, p.519).

2.2.4.4 The Sustained Attention to Control Task (SART)

A computer-based version of the SART was used to measure sustained attention (SART; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) and the 'inhibition' component of EF (Stevenson, Russell & Helton, 2011). In this continuous performance

reaction-time task, numbers 1-9 (GO trials) are presented in on a screen in a repeating fixed numerical order (1, 2, 3, 4, …). Participants are required to left-click the mouse (labelled 'YES') every time a number is presented onscreen (GO trials), except in the case of the number 3 (NO-GO trials), where they are required to withhold their response and wait for the next number. Numbers appear in white against a black screen, with each number remaining on-screen for 300ms, followed by an inter-stimulus interval of 800ms, when a white fixation cross was presented in the centre of the screen. The size of the stimuli was varied across the trial, to prevent participants from fixating on stimuli characteristics. 23 repetitions of the cycle of digits 1-9 were completed, giving 207 trials in total. The task lasted approximately 4 minutes.

Outcome variables:

Commission errors: incorrectly responding to NO-GO trials (i.e. number 3); purportedly reflects lapses of sustained attention

Omission errors: failure to respond to GO trials (numbers 1-2, 4-9); also reflect lapsing attention indicated by a break from task engagement.

2.2.4.5 The Choice Reaction Time Task (CRT)

This is a computer-based test designed to measure "speed of processing". The specific variant employed in the present study was deployed previously in the Irish Longitudinal Study of Ageing (Cronin et al., 2013). Participants were required to press a central start button on the PST Serial Response Box, and wait for a stimulus ('YES' or 'NO') to appear onscreen (Figure 2.2-7 below). This is a self-initiating test, and thus it will only proceed when the Start button is pressed and held. The stimulus appeared at random intervals 500-800ms after the Start button was pressed. Upon stimulus presentation, participants had to release the start button and press a corresponding YES or NO button located on the left (YES) or right (NO) of the response box (i.e. using the same digit). After a 10-trial practice block, the full task lasted for 100 trials (approximately 4 minutes). It has been shown previously that the "Cognitive Reaction Time" element of the task (see outcome variable description below) is an independent predictor of Timed Up and Go (TUG) performance in a sample of older Irish adults (Donoghue et al., 2012).

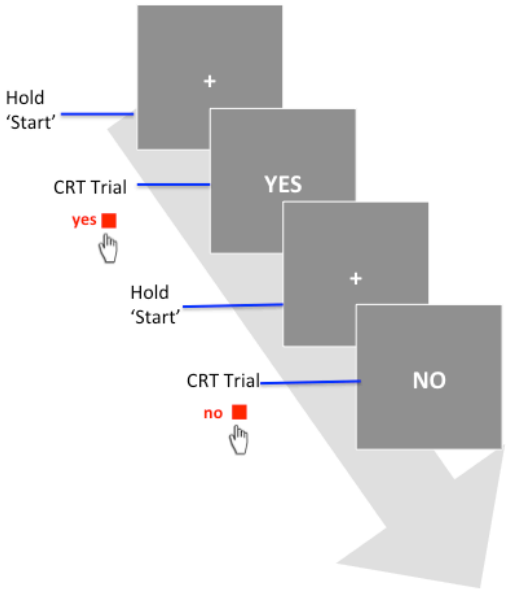

Figure 2.2-6 Schematic of the Choice Reaction Time Task: participants were required to hold down a start button until a stimulus appeared onscreen. They then had to quickly respond by pressing the corresponding button on a response box. To Start the next trial, they returned to the start button and held it down until the next stimulus appeared.

Outcome variables:

There are 2 components. The first is the time that elapses from the presentation of the stimulus to the release of the Start button. This is often referred to as the "Cognitive Reaction Time", and is typically interpreted in terms of processes concerned with decision-making and movement planning. The second component is the time that elapses from the release of the Start button, and the depression of the YES or NO button. This is often referred to as the "Motor Reaction Time" (e.g. Roberts & Pallier, 2001), although it would more generally be considered a measure of movement (execution) time.

2.3 Physical Measurements

Grip strength of both hands was measured using a digital hand dynamometer (Jamar). After a practice demonstration, participants were instructed to squeeze the handle of the dynamometer as hard as possible, and then over 3 seconds were instructed to increase force in order to ensure maximal force was recorded. Participants carried out the task with their left hand first, followed by their right (dominant) limb. The maximum value obtained across all three sessions (pre/post/retention) was used as a measure of maximum Grip Strength.

Dexterity was measured using the 9 Hole Pegboard Task (Rolyan® 9-Hole Peg Test), in which participants were instructed to place pegs one-by-one from the dish into 9 holes, then immediately replace them in the dish. Participants were given a practice trial on both hands before being timed completing the task as quickly as possible with each hand. All participants carried out the task with their right hand first, followed by left.

2.4 Statistical Analyses

All statistical analyses were carried out using R statistical software (R Core Team, 2012). A Bayesian re-sampling (bootstrapping) approach was employed to obtain credible estimates of the parameter values. Traditional frequentist approaches to parametric significance testing generate hypothetical sampling distributions from the null hypothesis, sampled according to the same stopping intentions as the collected data (Kruschke, 2013; 2014) in order to assess the probability that the fictitious data would be more extreme than the observed data. Typically, a p-value is defined as 'the probability of finding the observed data in the null hypothesis were true. Put differently, the *p*-value is "the probability that fictional, counterfactual data from the null hypothesis would be more extreme than the observed data, when those data were sampled and tested as intended by the current researchers" (Kruschke & Liddell, 2017, p.5). Thus, rather than relying on a hypothetical extreme distribution, Bayesian approaches rely on credible *intervals* based on prior theory and the observed data. Therefore a Bayesian approach, based directly on posterior credible intervals, is more intuitive and more credible (Kruschke, 2014).

Bootstrapping is a method of estimating the precision of parameter variables (i.e. parameter values that mathematically describe the data, such as medians, means, variances, etc.) by drawing randomly with replacement from an approximating distribution. Bayesian approaches to re-sampling use only the observed data in their parameter estimates. They create new datasets by reallocating or 're-weighting' the initial data, with Bayesian analysis providing the mathematical formula for the reallocation. Bayesian analysis gives us an explicit distribution of credibilities of the parameter values across the range of possible values. Initially, we begin with a prior distribution of the parameter values, based on prior knowledge, and then consider the new data we have collected in order to arrive at a posterior distribution of the parameter values. If there is no prior knowledge, un-informative prior distributions can be specified that have little influence on the posterior distribution. The posterior distribution assigns greater credibility to values that are consistent with the data (Krusckhe & Liddell, 2017). This posterior distribution gives us the credibility of every single parameter value, and can indicate which parameter values are most credible (i.e. the mode of the distribution). It also gives us the range of parameter values that cover the most credible set of values (known as the 'Highest Density Interval', or HDI). For example, if the 95% HDI

indicates that most credible values of the mean, μ , lie between 10 and 15, then we would state a belief that the mean μ has 95% probability of falling between 10 and 15.

For a given parameter, the posterior distribution can be approximated using re-sampling techniques. Markov chain Monte Carlo (MCMC) is a method of sampling probability distributions that can generate confidence (credible) intervals when assumptions of normality are violated. Measuring the properties of a target distribution by generating samples of representative random values from the distribution is called Monte Carlo simulation. A Markov chain is a 'directed random walk' through a parameter space that includes all the possible values of the parameter we are interested in. The term random walk indicates that each step in the parameter space is independent of the previous steps. A chain of such steps, in which the current step has no memory for previous states, is called a Markov Chain. The term 'directed' is used to imply that although the next value in the chain is selected at random, some values are more likely to be drawn than others, in proportion to their probability (which is determined by both the data and the prior distribution) (Hamra, MacLehose, & Richardson, 2013). In other words, the chain is more likely to 'walk around' more important areas of the parameter space. We can thus reconstruct the distributions of the parameter, and these sample distributions mimic samples from the true posterior. The Central Limit Theorem dictates that with sufficient resampling, Monte Carlo estimates approach normality, regardless of the distribution characteristics of the original sample. Additional benefits of this approach are that they do not require equal group size, are less adversely affected by missing data and can be used with data that are not normally distributed.

The analysis was implemented in R using the MCMCglmm package (Hadfield 2010) to fit Generalised Linear mixed models using Markov Chain Monte Carlo techniques. An unspecified variance–covariance matrix was used for random effects and residuals, to allow unconstrained correlations in the random effects and residuals. As we had no prior information about the covariance matrix in advance of analysis, weakly informative inverse Wishart priors were used for the random and fixed effects. These priors should have a minimal influence on the posterior distribution. For all cognitive outcomes measures, 100,000 iterations (samples) of the model were undertaken. The size of the sample should be such that the estimates are accurate and stable (Kruschke, 2014), i.e. if the MCMC analysis was run again, the 95% HDI should not be much different. The 'thinning interval' was set at 10. The thinning interval is a method of reducing the chance of autocorrelation among iterations. The thinning interval specifies the MCMCglmm procedure to only keep every 10^{th} value in the sampling process, in order

to reduce autocorrelation, as samples that are near each other in the sampling process are more likely to be correlated. The 'burn-in' period, which instructs the procedure to ignore the initial samples, was set to 10,000. This is important as we do not want the sample to be unduly influenced by the random starting point of the Markov chain. The resulting effective sample size was 9,000 for each parameter.

Model Diagnostics: The mathematics of MCMC imply that infinitely long chains of samples will attain perfect representations of the posterior distributions, however due to limited time and computer memory, a sample size must be decided upon. Thus, the quality of our infinite MCMC chain must be checked for signs of unrepresentativeness or instability. A number of steps were taken to assess the stability and adequacy of the obtained posterior distributions. One method is to run the MCMC analysis with different starting points, and the resulting chains should 'converge' with or overlap each other. Visual inspection of trace and density plots were examined to assess convergence. In addition, Gelman and Rubin diagnostics (Gelman & Rubin, 1992) were run to obtain the Potential Scale Reduction (PSR) factor to ensure 'convergence' was achieved within each model. The PSR is a numerical check of the variance between chains, with values near 1 indicating adequate convergence.

Planned Contrasts: Scores obtained prior to the intervention (pre), following the intervention (post) and at a retention session following a period of no training (ret) were compared for all cognitive outcome variables, and the results of planned contrasts were summarised using least-square means tables. Least square means and pairwise contrasts for the MCMCglmm model were calculated using the lsmeans() package (Lenth & Hervé, 2015). Corrections for multiple comparisons were not necessary, as by utilising Bayesian analyses, we are not basing our decisions on error control or sampling distributions, but on the properties of the posterior distributions of the parameter values (Krushcke and Liddell, 2017). We are making direct comparisons between two sets of data, and the use of multilevel models allows us to capture the common influences. In addition, the prior distribution regulates any point estimates. In all cases, separate analyses were carried out for the intervention (Motor Training) and active control (Control) groups.

2.4.1 Effect Size Estimates

Cohen's *f* was calculated as a measure of effect size for each of the planned contrasts (Cohen, 1988). Cohen suggested that *f* values of 0.1 indicate a small effect size, values of 0.25 indicate a medium effect size, values of 0.4 or over are indicative of a large effect size. This standardized measure of effect size allows us to compare the effects of the different conditions on the different outcome measures and assists in the interpretation of the p-value. In order to confidently infer that reliable changes were seen after the training, we imposed the criteria that in order to be considered reliable, p-values must fall below 0.05, and in addition, effect sizes must be medium to large (i.e. Cohen's $f > 0.25$).

2.4.2 Model fitting: Deviance Information Criterion

The Deviance Information Criterion (DIC) as a method of Bayesian model comparison is based on a trade-off between how well the data fit the model, and the corresponding model complexity (Spiegelhalter et al, 2002), DIC= Goodness of fit + complexity, where:

$$\mathrm{DIC} = D(\bar{\theta}) + 2_{p_D}$$

Where 'Deviance', $D(\bar{\theta})$, measures the 'goodness of fit' of the model:

$$D(\bar{\theta}) = -2\mathrm{logL}(\mathrm{data}|\theta)$$

and model complexity is measured by the second half of the equation, where p_D is a measure of the effective number of parameters in the model, defined as the posterior mean deviance, $\bar{D}$, minus deviance obtained at the posterior mean of the parameters, $D(\bar{\theta})$:

$$p_D = \bar{D} - D(\bar{\theta}).$$

Models with smaller DIC are better supported by the data, and thus all models used herein were selected on the basis of having an optimal DIC.

2.4.3 Dealing with outliers: Adjusted boxplots

In order to visualize the distribution of the data and identify any outliers, an adjusted version of the boxplot is used that is suitable for use with skewed data (Hubert

and Vandervieren, 2008). In traditional boxplots, the whiskers are located at the points calculated using the following equations:

$$Q_1 - 1.5* \text{IQR} \quad \textit{(lower whisker)}$$
$$Q_3 + 1.5* \text{IQR} \quad \textit{(upper whisker)}$$

where IQR stands for the Inter Quartile Range, Q1 is the 25th percentile of the data, and Q3 is the 75th percentile of the data. Under this rule, anything lying outside the whiskers as a potential outlier. However, a weakness of this method is that as the length of the two whiskers are identical, it is only appropriate to use it when the distribution of the data between the two intervals is normally distributed. It is popular to overcome this shortcoming by transforming the data until it approximates a Gaussian distribution. However, this can cause problems for the interpretation of the data at later stages of the analysis. An alternative approach is to adjust the rule used to calculate the whiskers.

Adjusted boxplots include a measure of skewness in the equation, and allow the length of the whiskers to vary in line with the skewness of the data, using the following equation:

$$Q_1 - \exp(M, \alpha)1.5* \text{IQR} \quad \textit{(lower whisker)}$$
$$Q_3 + \exp(M, \beta)1.5* \text{IQR} \quad \textit{(upper whisker)}$$

where M is a measure of skewness (the authors suggest using the medcouple, a scaled median difference of the left and right half of the distribution), and α and β are scaling factors that determine the outlier boundaries, chosen to ensure that for skewed distributions without outliers, the probability of falling outside the whiskers is relatively small. In the present implementation, both were set to 1.5, indicating the whiskers extended to the most extreme data point which was no more than 1.5 times the IQR from the box. If the data is not skewed, then M is reduced to zero, and the classic equation is used.

2.4.4 Data Visualization with Pirate Plots

A pirate plot is a way of plotting data that shows critical distributional information. Pirate plots, like traditional bar-charts, display central tendencies, but also include important information about the raw data and its distribution, which are hidden in traditional bar-charts (Figure 2.4-1). They display all the raw data points, jittered around the centre for optimal visualisation; and a smoothed density plot or 'bean plot'

which illustrates the density/ crowdedness or sparseness of the data at each possible value. Finally, they include a rectangle around the central tendency (i.e. the mean), which represents an 'inference interval' (here a Bayesian Highest Density Interval, but can also be set to frequentist confidence intervals). A Bayesian 95% Highest Density Interval covers 95% of the probability density for the posterior distribution. As the HDI includes 95% of the posterior distribution, the width of the HDI indicates the level of certainty of our beliefs; if it is wide, there is less certainty, and if it's narrow, then we can be more certain about our beliefs (Kruschke, 2010).

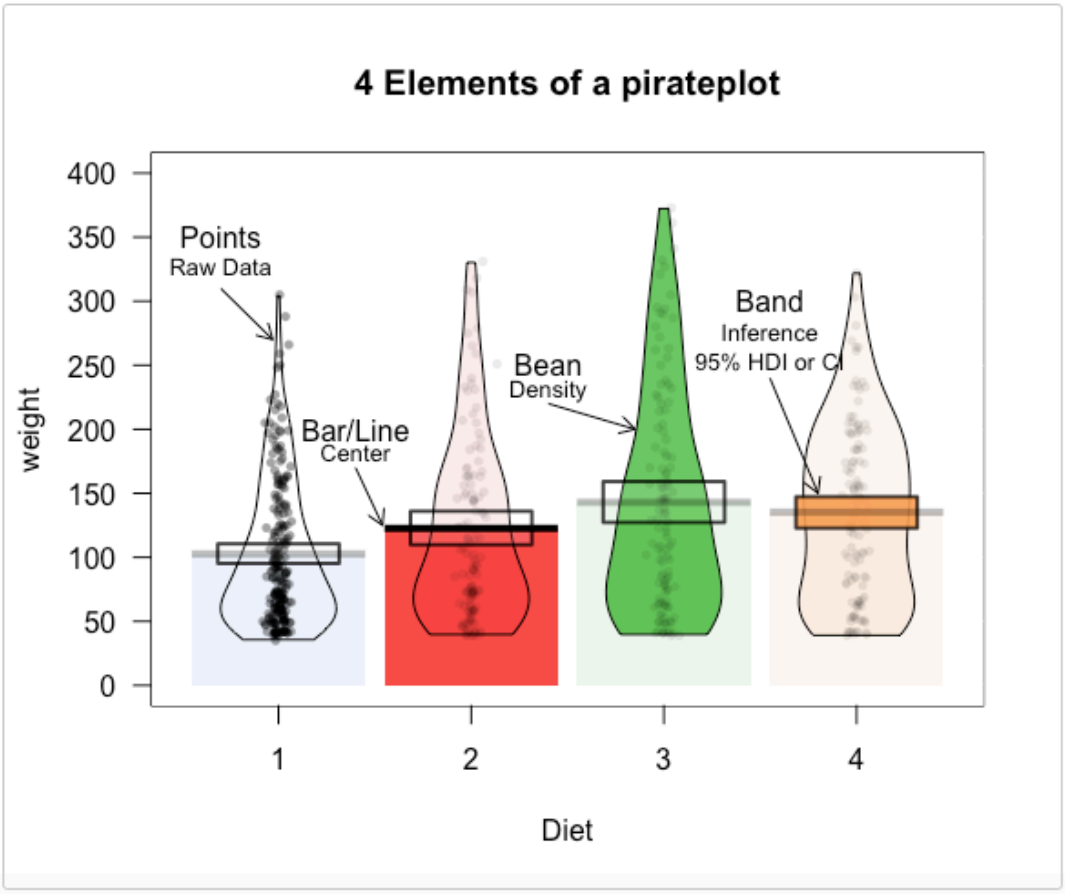

Figure 2.4-1. Graph illustrating the four elements of a Pirate Plot. Point (1). Illustrates all the raw data points behind each group, and points are horizontally jittered, to give the viewer information about the spread of the raw data. This is useful in spotting outliers or suspicious gaps in the raw data. Point (2) on the x-axis shows the Bar or Line depicting the measure of central tendency, as in traditional bar-charts. Point (3) illustrates a smoothed density line depicting a sideways density plot. This is also known as a 'bean' plot, and informs the viewer about the how dense/crowded or sparse data are at each value. Finally, point (4) on the x-axis utilises the BEST package to generate 95% HDIs of each mean; and we can state that there's a 95% probability that this interval contains the true population mean. Inferences can be made by looking at the HDIs; if they do not overlap, we can state with high confidence that the group means are different. [Image downloaded from cran.r-project.org/web/packages/yarrr/vignettes/pirateplot.htmlin November 2017.]

2.5 Cognitive Task Results

2.5.1 Summary

At the post-intervention testing session, changes were seen in performance on some measures of cognitive function (See Table 2.5.1 below for a simple visual summary). Changes were seen in performance on the Choice Reaction Time task (CRT) for the training group only at post-intervention, and both groups showed improvements on certain measures on the SART and n-Back tasks.

Table 2.5.1 Simple visual representation of changes in performance on the cognitive measures at the post-test session. The green arrow indicates improved performance, whereas the tilde indicates no reliable changes in performance were demonstrated.

Cognitive Test	Training Group	Control Group
SART Errors	↓	↓
CRT	↓	~
Flanker	~	~
TMT	~	~
n-Back & Dual n-Back	↓ ~	↓ ~

- **Choice Reaction Time Task**: Training group RTs were reliably lower for both the Cognitive RT and the Motor RT scores. This effect was not seen for the Cognitive RT at the retention session, however Motor RTs were remained reliably lower for the training groups participants at the retention session. No changes were seen for the control group on either measure of performance on the CRT at the post or retention test sessions.

- **Sustained Attention to Response Task:** Both groups improved on the Sustained Attention to Response Task after the intervention period. Bothe groups made fewer commission errors at both the post- and retention-test sessions. Only the training group showed improvements on the number of

Omission errors made, displaying fewer errors at the post-test session. No reliable differences were seen at retention.

- **n-Back and Dual n-Back**: Both traning and control groups improved on some subtasks of the n-back and dual n-back tasks. The training group primarily exhibited improvements in the RT measures. Conversely, the active control group tended to show improvements in the accuracy measures derived for these tasks. In relation to the visuospatial n-Back task, no changes were seen in the easiest '1-back' task condition, in terms of either accuracy or RT measures for either group. In the 2-back condition, the control group improved reliably on measures of visual accuracy. In the Dual n-back task, the motor training group improved performance on the reaction time measures, both visual and auditory, whereas the control group showed no improvement on these measures. The control group improved on measures of auditory accuracy in the 2-back condition at the post-test session.

No reliable differences were seen in the flanker task or the Trail Making Task performance post-intervention or at the retention session for either the training or control group.

2.5.2 Montreal Cognitive Assessment (MoCA)

Participants scored an average of 27.27 on the MoCA, with Median score 27 and Standard deviation of 1.86. Scores ranged from 21-30. Using 23 as the cut-off score for potential mild cognitive impairment (as recommended by Carson, Leach & Murphy, 2017), one participant was identified as falling below the threshold, with a score of 21. The participant (ID 112) was excluded from all further analysis.

2.5.3 Flanker Task

2.5.3.1 Conflict Cost

Data Cleaning:

Conflict cost scores were calculated by subtracting the Median RT for congruent trials from the Median RT for the incongruent trials. Adjusted boxplots (Hubert and Vandervieran, 2008) revealed no outliers for the training group conflict cost scores, and in the control group 2 values falling outside the extreme upper fence (121.7) were identified (one post-test score, one pre-test score), and 1 value falling below the lower extreme fence (-82.8) was identified (post-test score). Outliers were removed prior to further analysis.

Analysis:

In the MCMCglmm model, Time were included as fixed effect, with Gender included as a covariate. Participants crossed with time (levels = pre, post, retention) was a designated random effect, and Age was included in the model as a covariate (random effect), as the DIC indicated better model fit including Age and Gender. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's f) were calculated.

While the Median conflict cost decreased more in the Training group (see Table 2.5-3), no evidence supported the conclusion that Motor Training had an impact on performance of the flanker task. For all pre-post and pre-retention contrasts, no difference in pre-post session conflict cost score was seen for either the motor training group or the active control group.

Table 2.5-3 Pre-Post and Pre-Retention Contrasts for Flanker Median Conflict Cost

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	30.9 (11.1)	21 (10.9)	28.6 (10.9)	0.462	0.12	38	0.862	0.01	38
Control	40.5 (10.3)	36.4 (10.5)	47.7 (9.9)	0.741	0.06	32	0.547	0.05	32

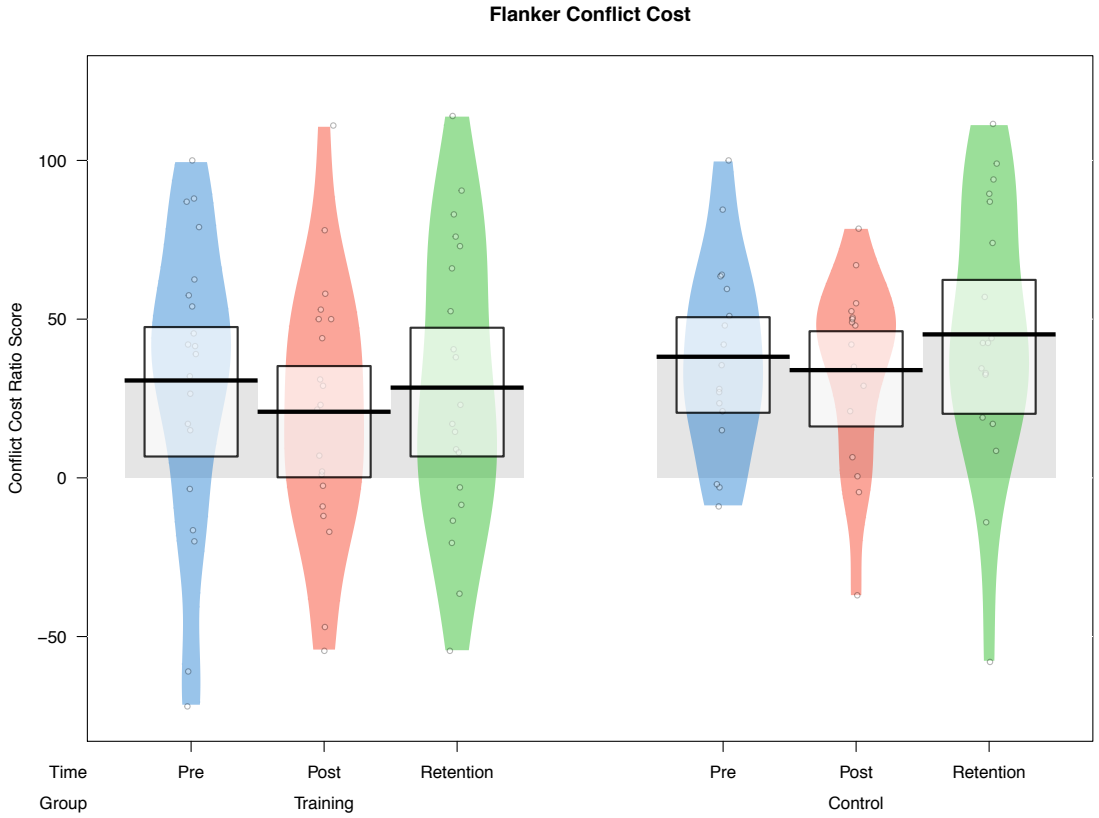

Figure 2.5-1 Conflict cost scores across sessions for both the training and control groups. Conflict cost is the Median RT for incongruent trials minus the Median RT for congruent trials. In all cases, the 95% Highest Density Intervals overlap substantially, supporting the conclusion that there were no reliable differences across training sessions for either training or control groups.

2.5.4 Choice Reaction Time (CRT)

2.5.4.1 Cognitive Reaction Time

Data Cleaning:

Cognitive Reaction Time scores were calculated as the median reaction time taken to release the Start button after the appearance of the Yes/No stimulus onscreen. Two outliers were identified using the adjusted boxplot methods, originating from one participant in the training group (pre-test). These two values fell outside the upper extreme fence value (676.4ms). What follows is a summary of the results with the outliers removed.

Model:

In the MCMCglmm model, Time and Target (levels = yes, no) were included as fixed effects, with Gender included as a covariate. Participants crossed with time (levels = pre, post, retention) was a designated random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the DIC. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's f) were calculated.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups revealed a decrease in Cognitive Reaction Time for pre-post contrasts (p = 0.001, f = 0.41) and the pre-retention contrasts (p = 0.002, f= 0.18) in the training group only. However, a large effect size was only seen in the difference between pre-and post-test scores. No changes in median RT were found in the control group across pre-post or pre-retention contrasts.

Table 2.5-4 Pre-post contrasts for the median Cognitive Reaction Times (ms)

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	487(26)	439(26)	443(26)	**.000***	**0.41**	79	**.002***	0.18	79
Control	489(37)	481(37)	471(37)	.048	0.08	77	.119	0.09	77

* indicates p<0.05. Medium and large effect sizes (Cohen's f >0.25) in bold.

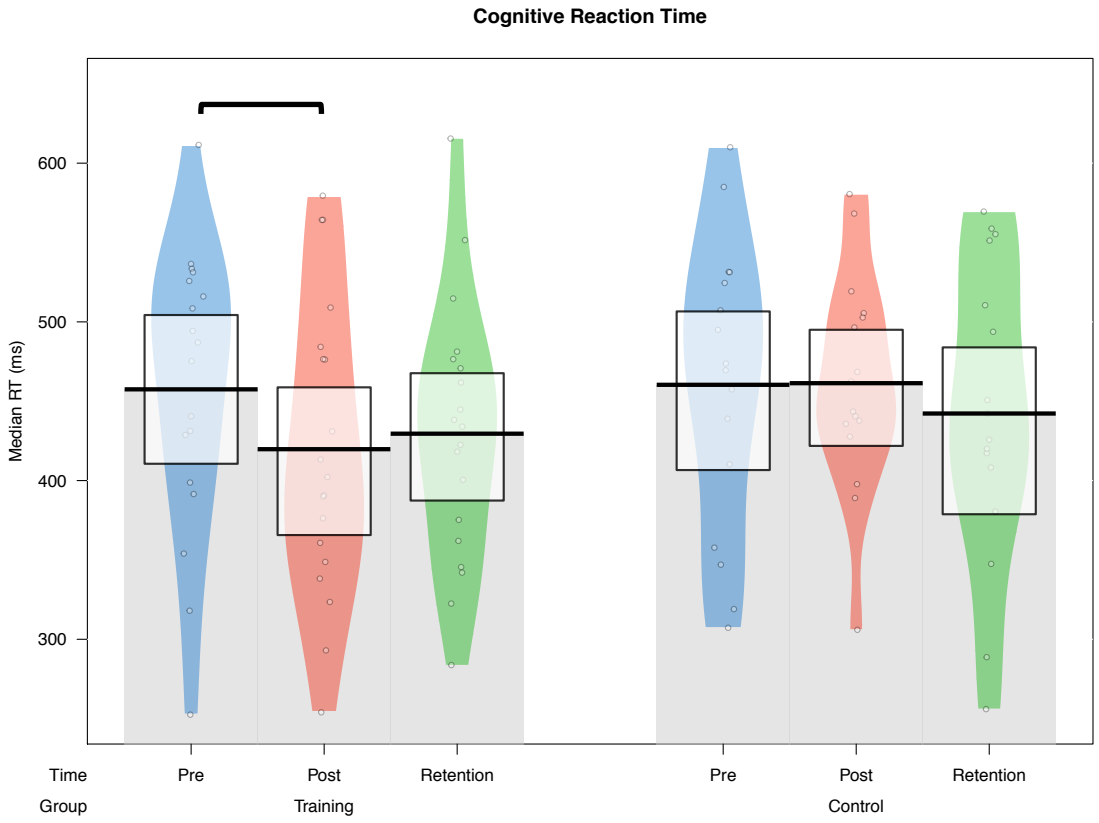

Figure 2.5-2 Pirate plot showing the Cognitive Reaction Times for Training and Control groups. For the training group, cognitive RT is lower following the motor training intervention, as can be seen by a notable difference between the 95% HDIs. No other changes were reliably observed.

2.5.4.2 Motor Reaction Time

Data Cleaning:

Seven outliers were identified in Motor RT data using the adjusted boxplot methods, falling outside the upper extreme fence value (598.4ms). Detected outliers originated from two participants in the control group (2 pre, 3 post, 2retention). Outliers were removed prior to analysis.

Analysis:

Median motor RT was lower following the intervention than in the pre-test session for the training group only. The effect size index indicated a medium effect size for this difference ($p = 0.018$, Cohen's $f = 0.27$). No significant changes in motor RT were observed across Time for the control group. Looking at differences in motor RT between the pre-test session and the retention, the median motor RT remained lower in

the retention session for the training group, however the effect size was small (p=0.045, Cohen's *f*= 0.11). No reliable changes in motor RT were seen for the control group.

Table 2.5-4 Pre-post contrasts for the median Motor Reaction Times (ms)

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	374(21.5)	337(21.6)	342(21.8)	**0.018***	**0.27**	79	**0.045***	0.11	79
Control	362(39.7)	336(39.5)	319(39.7)	0.254	0.14	71	0.055	0.11	71

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

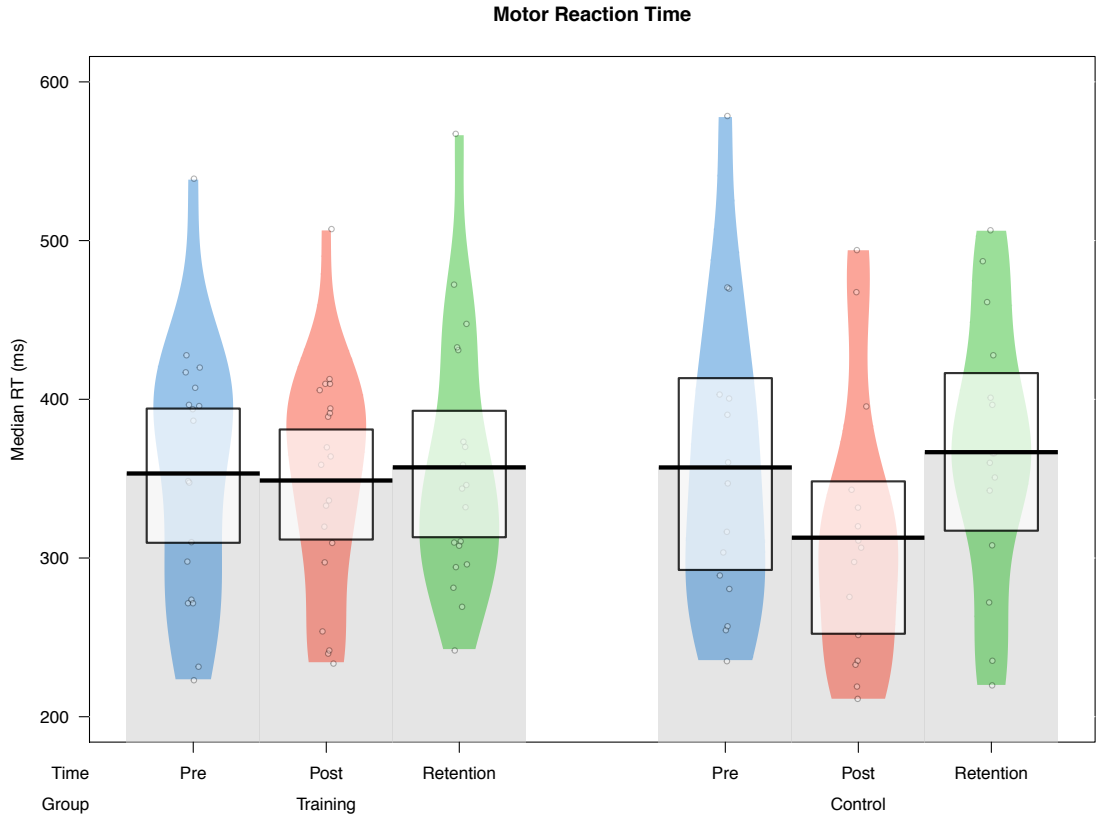

Figure 2.5-3: Pirate plot showing the median Motor Reaction Times for Training and Control Groups. For the Training group, the widest part of the 'bean' gets lower across the testing sessions. However, across all sessions, the centre line falls within the 95% HDI for the other groups, indicating no reliable changes.

2.5.5 n-Back and Dual n-Back

Data Cleaning:

Reaction times below 150ms were excluded form RT data analysis. Incorrect responses were also removed from the RT data analysis. Adjusted boxplots detected no probable outliers for any of the accuracy or median RT scores across auditory or visual domains. In the visuospatial n-Back (single) task, results are reported separately for the 1-back and 2-back trials. In the dual task, Reaction Time data and Accuracy data were recorded separately for both visual and auditory stimuli, and for both 1-back and 2-back trials.

2.5.5.1 Accuracy

Accuracy scores were calculated for each of the four conditions, trial (1-back, 2-back) by stimulus type (auditory, visual) by subtracting the number of misses from the number of hits (Jaeggi et al., 2008); this performance index is known as the discrimination index.

Visual Accuracy: Visuospatial Task

For the one-back task, accuracy scores following the intervention were not markedly different at post-training for either the training group or the control group. Similarly, accuracy scores could not reliably be distinguished from pre-test performance at the retention session. Means and standard errors can be seen in Table 2.5-5 below. In the 2-back task, only the control group accuracy scores were higher post-intervention (p=0.013, Cohen's *f*= 0.32). In addition, higher accuracy scores on the dual 1-back task were seen at retention compared to pre-test for the training group only (p=0.003, Cohen's *f* = 0.28).

Visual Accuracy: Dual Task

For the dual one-back task, accuracy scores following the intervention were higher at post-training for the control group (p=0.017, Cohen's *f*= 0.39), whereas in the training group the increase in accuracy performance approached conventional levels of statistical significance, however a medium effect size was observed (p=0.079, Cohen's *f*= 0.33). At retention, accuracy scores were reliably higher than pre-intervention scores for the training group only (p=0.003, Cohen's *f* =0.28). In the most difficult task condition, the dual 2-back, accuracy performance post-intervention did not differ from

pre-intervention scores for either training or control groups. However, at retention, the training group showed improved accuracy scores compared to their pre-test performance (p=0.002, Cohen's *f*= 0.26). Means and standard errors can be seen in Table 2.5-5 below.

Auditory Accuracy: Dual Task

For the 1-back task condition, no consistent changes in auditory accuracy were observed across sessions for either the training or control groups. In the 2-back condition, the control group accuracy scores were higher post-intervention (p=0.017, Cohen's *f* = 0.35). No consistent changes in 2-back auditory accuracy were seen across sessions for the training group.

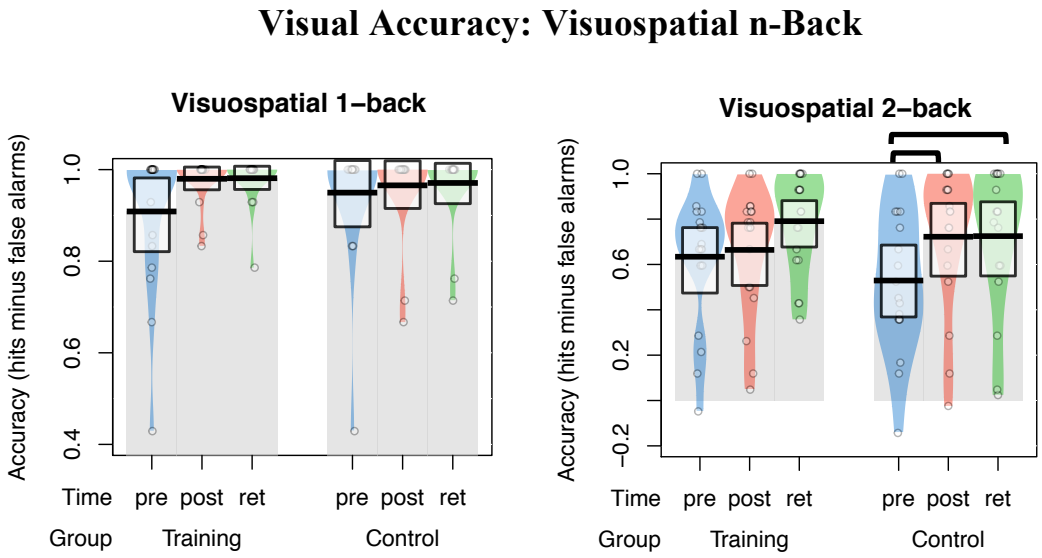

Figure 2.5-4: Pirate Plot showing the Visual Accuracy scores for Training and Control groups in the Visuospatial 1-back and 2-back tasks. In the visuospatial 1-back, no reliable differences can be observed across session for the training and control group. In the 2-back condition, the 95% HDIs for the control group post-test and retention-test accuracy scores fall above the pre-test 95% HDI, indicating improved accuracy performance on the task. Thus the control participants improved on VS 2-back performance at the post and retention-test sessions.

Visual Accuracy: Dual n-Back

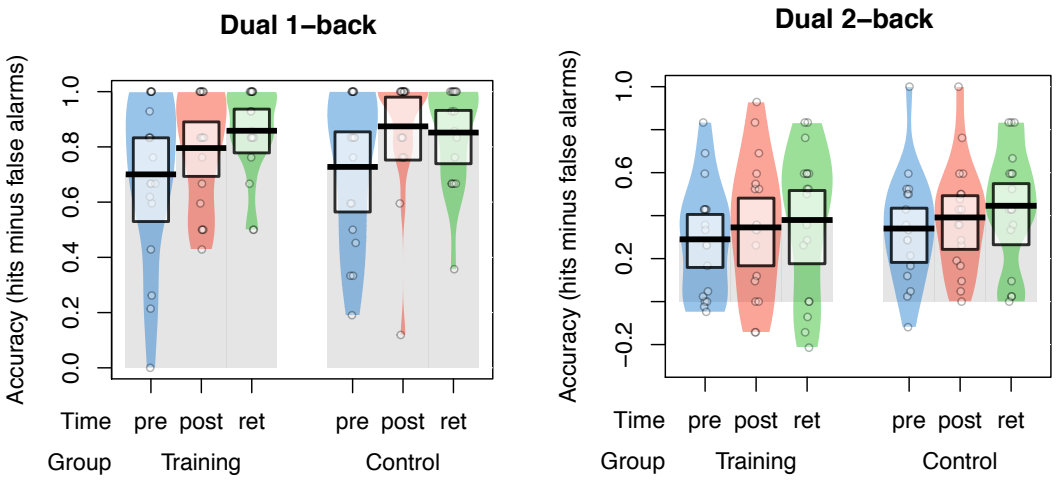

Figure 2.5-5 Pirate Plot showing the Visual Accuracy scores for Training and Control groups in the dual 1-back and dual 2-back tasks. In the dual 1-back, the majority of the control group 95% HDI in the post-test session falls above the pre-test interval, indicating improved performance post-intervention. For the training group, the majority of the 95% HDI in the retention-test session falls above the pre-test interval, indicating improved accuracy performance at retention. In the 2-back condition, no reliable differences are seen across session for the training group, and for the controls, the 95% HDIs for the retention-test accuracy scores fall above the pre-test 95% HDI, indicating improved accuracy performance at retention.

Auditory Accuracy: Dual n-Back

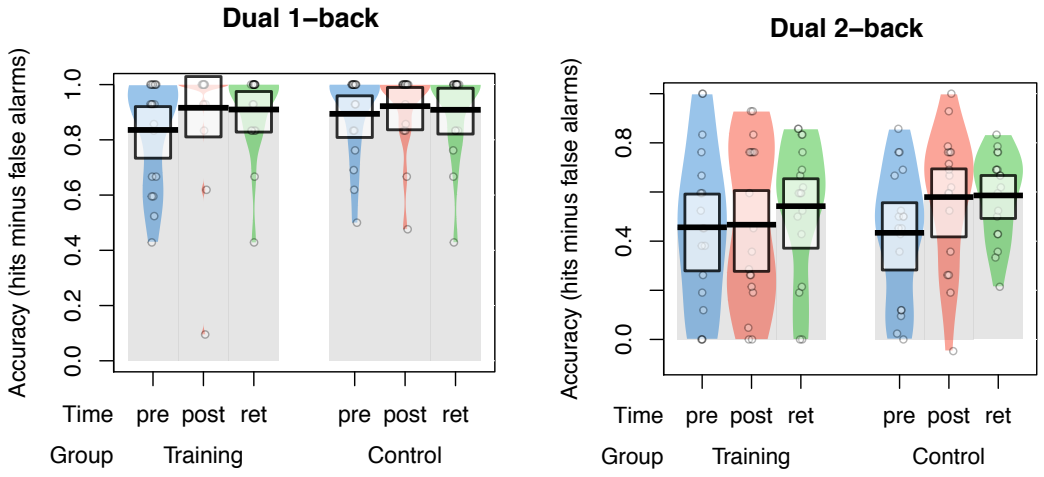

Figure 2.5-6 Pirate Plot showing the Auditory Accuracy scores for Training and Control groups in the dual 1-back and dual 2-back tasks. No reliable differences across session can be observed from the bean plots in the dual 1-back task condition. For the dual 2-back, the control group show higher accuracy scores at post and retention sessions, with their 95% HDIs falling above the pre-test interval, indicating reliable performance improvements on the auditory accuracy measures

Table 2.5-5 Visual Accuracy Scores on the Visuospatial and Dual n-Back Tasks.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Visuospatial	1	.902 (.066)	.973 (.065)	.974 (.065)	0.191	0.38	36	0.190	**0.37**	36
		2	.627 (.066)	.657 (.066)	.784 (.066)	0.589	0.08	36	**0.004***	0.19	36
	Dual	1	.693 (.065)	.789 (.065)	.852 (.066)	**0.079***	**0.33**	36	**0.003***	**0.28**	36
		2	.289 (.069)	.389 (.072)	.485 (.072)	0.103	**0.30**	27	**0.002***	**0.26**	36
Control	Visuospatial	1	.967 (.068)	.983 (.067)	0.988 (.069)	0.800	0.12	33	0.734	0.08	33
		2	.585 (.069)	.739 (.068)	0.742 (.069)	**0.013***	**0.32**	33	0.012*	0.16	33
	Dual	1	.745 (.068)	.892 (.068)	.869 (.068)	0.017*	0.39	34	0.042*	0.17	34
		2	.358 (.068)	.405 (.068)	0.466 (.069)	0.448	0.16	33	0.083*	0.15	33

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

Table 2.5-6: Auditory Accuracy Scores on the Dual n-Back Task.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Dual	1	.825 (.073)	.905 (.073)	.899 (.073)	0.233	**0.34**	36	0.278	0.16	36
		2	.464 (.078)	.461 (.077)	.544 (.076)	0.968	0.02	31	0.267	0.06	31
Control	Dual	1	.887 (.062)	.906 (.062)	.892 (.061)	0.582	0.11	34	0.770	0.03	34
		2	.436 (.062)	.566 (.060)	.569 (.060)	**0.017***	**0.35**	33	0.014*	0.17	33

* indicates p<0.05. Medium and large effect sizes (Cohen's f >0.25) in bold.

2.5.5.2 Reaction Time

Visual Reaction Time: Visuospatial Task

No reliable systematic changes in visual RTs were observed in either the training or control groups across pre-/post/retention-test sessions, for either the 1-back or 2-back conditions. In the 2-back condition, the control group RT *increased* and this increase was accompanied by a medium effect size, however this change did not reach conventional levels of statistical significance.

Visual Reaction Time: Dual Task

In the dual 1-Back task, no systematic differences were observed between pre- and post-test visual RT performance. Comparing retention performance to pre-intervention performance, a decrease in RT was observed for the training group (p=0.009), however the effect size was categorised as small, (Cohen's f= 0.24), falling just below the cut-off score for medium effect size ($f \geq 0.25$). In the dual 2-back task, consistent reductions in RT were again only observed for the training group, both at post-test (p=0.026, Cohen's f= 0.24), again falling just shy of a medium effect size. No reliable differences in 2-back visual RT were observed across sessions for the control group. Medians and standard errors can be seen in Table 2.5.7 below.

Auditory Reaction Time: Dual Task

In the dual 1-back task, the training group auditory RT scores were lower at the post-intervention session compared to the pre-test, and this was designated a large effect (p=0.009, Cohen's f= 0.43). No reliable differences in auditory RT were observed in the control group for the 1-back task. For the dual 2-back task, no systematic changes in auditory RT were observed across session in the training or control conditions.

Table 2.5-7 Visual Reaction Time on the Visuospatial and Dual n-Back Tasks.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Visuospatial	1	642(75.8)	575(76.8)	583(76.4)	0.394	**0.28**	36	0.458	0.12	36
		2	846(76.6)	721(77.2)	794(77)	0.111	**0.25**	36	0.510	0.05	36
	Dual	1	1384(75.2)	1285(76.5)	1180(76.6)	0.207	**0.23**	36	**0.009***	**0.24**	36
		2	1833(81.1)	1637(84.4)	1654(87.1)	**0.026***	**0.24**	27	0.050*	0.12	27
Control	Visuospatial	1	592(82)	614(83.5)	618(83)	0.813	0.09	34	0.783	0.05	34
		2	752(85.8)	886(82.2)	733(82.9)	0.161	**0.36**	33	0.842	0.02	33
	Dual	1	1286(82.3)	1270(82.4)	1214(83.5)	0.864	0.03	34	0.440	0.07	34
		2	1599(82.9)	1464(84)	1455(85.6)	0.156	0.20	33	0.133	0.10	33

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

Table 2.5-8 Auditory Reaction Time on the Dual n-Back Task

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Dual	1	1301(103)	1002(103)	1070(104)	**0.009***	**0.43**	36	**0.044**	0.17	36
		2	1483(111)	1551(107)	1518(107)	0.573	0.09	31	0.773	0.02	31
Control	Dual	1	1071(97)	1130(96)	1027(97)	0.557	0.11	34	0.670	0.04	34
		2	1449(97)	1591(97)	1541(99)	0.170	0.20	33	0.380	0.06	33

* indicates p<0.05. Medium and large effect sizes (Cohen's f >0.25) in bold.

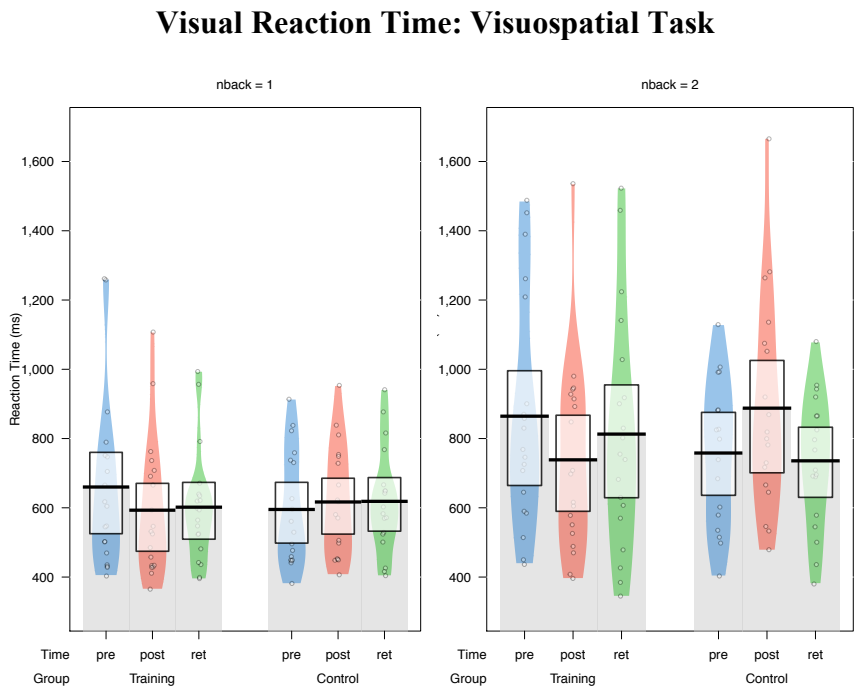

Figure 2.5-7 Pirate plot displaying the median Visual Reaction Time scores for the visuospatial 1-back and 2-back tasks. Only in the control group 2-back condition did the majority of the 95% HDI for the post-test visual RT fall above the 95% HDI of the pre-test score interval, indicating poorer performance. No other reliable changes across sessions were observed.

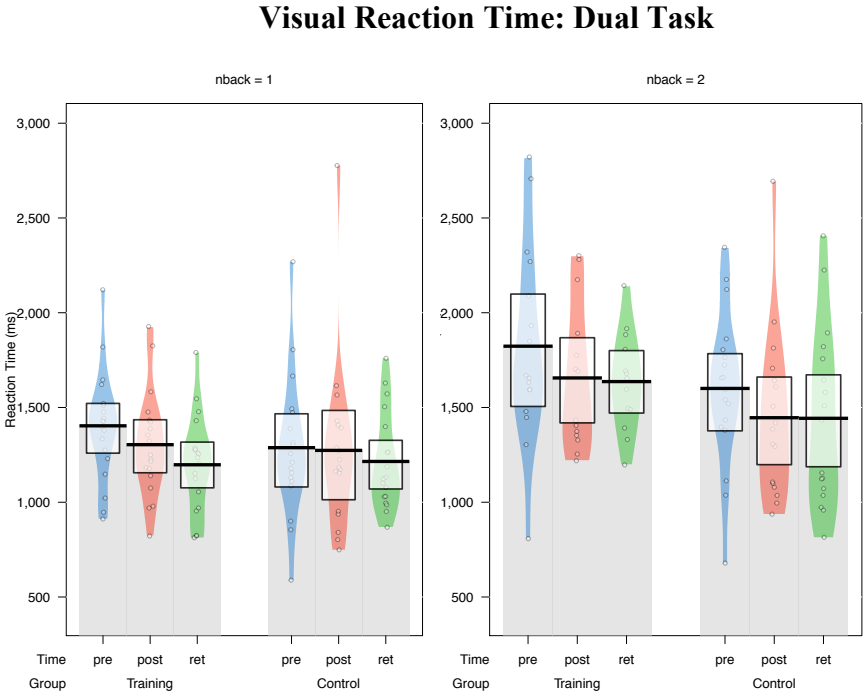

Figure 2.5-8 Pirate Plot displaying the median Visual Reaction Time scores for the dual 1-back and 2-back tasks. Only in the training group 1-back condition did the majority of the 95% HDI for the retention-test visual RT fall below the 95% HDI of the pre-test scores. No other changes across sessions were reliable.

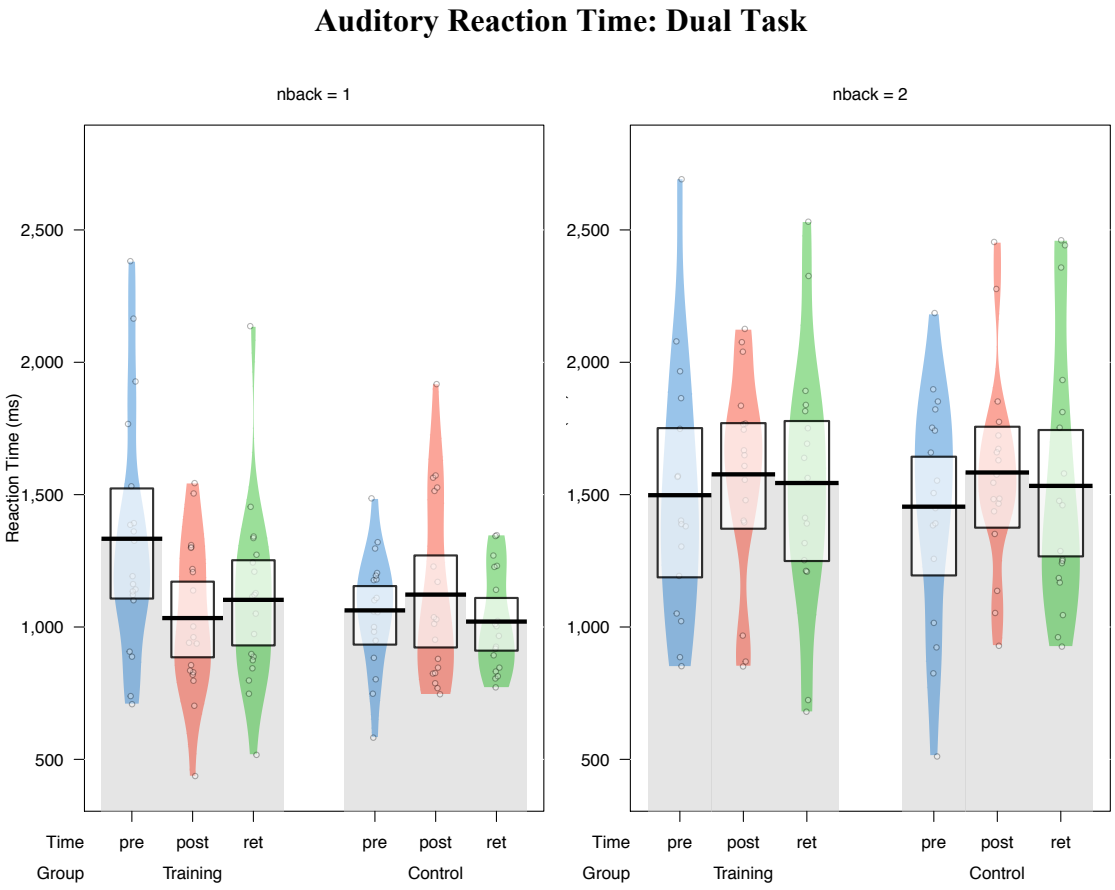

Figure 2.5-9: Pirate Plot displaying the median Auditory Reaction Time scores for the dual 1-back and 2-back tasks. Only in the training group 1-back condition did the majoity of the 95% HDI for the post-test auditory RT fall below the 95% HDI of the pre-test scores. No other changes across sessions were reliable.

2.5.6 Trail Making Task

In the Trail Making Task, participants carried out two Blocks of the TMT. Each block consisted of trial A and trial B, and participants carried out the tasks in an interleaved manner (i.e. trial order: A, B, A, B). Trial A consisted of numbers only (1-26), whereas Trial B consisted of numbers and letters (1-A-2-B etc.). The outcome variable was the median Reaction Time scores for Trial B divided by the median Reaction Time Score for Trial A; the 'B/A Ratio score'. Scores were calculated separately for each of the two blocks, but contrasts are reported on the combined results.

Data Cleaning:

The adjusted boxplot method identified no outliers in the training group, and one outlier in the control group (pre-test score falling below the lower extreme fence (< 0.89, post-test score, block 2). This outlier was removed prior to analysis.

Model:

In the MCMCglmm model, Time, and Block (levels = 1, 2) were designated fixed effects, with Gender included as a covariate. Participants crossed with Time (levels = pre, post, retention) were designated random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's ***f***) were calculated.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups revealed no reliable systematic changes in the TMT ratio scores across sessions for either the training group or the control group.

Table 2.5-9 Median B/A Ratio Scores on the Trail Making Task.

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	1.35 (.05)	1.31 (.050)	1.28 (.049)	0.460	0.08	92	0.174	0.07	92
Control	1.25 (.052)	1.23 (.052)	1.23 (.051)	.715	0.03	86	.717	0.02	86

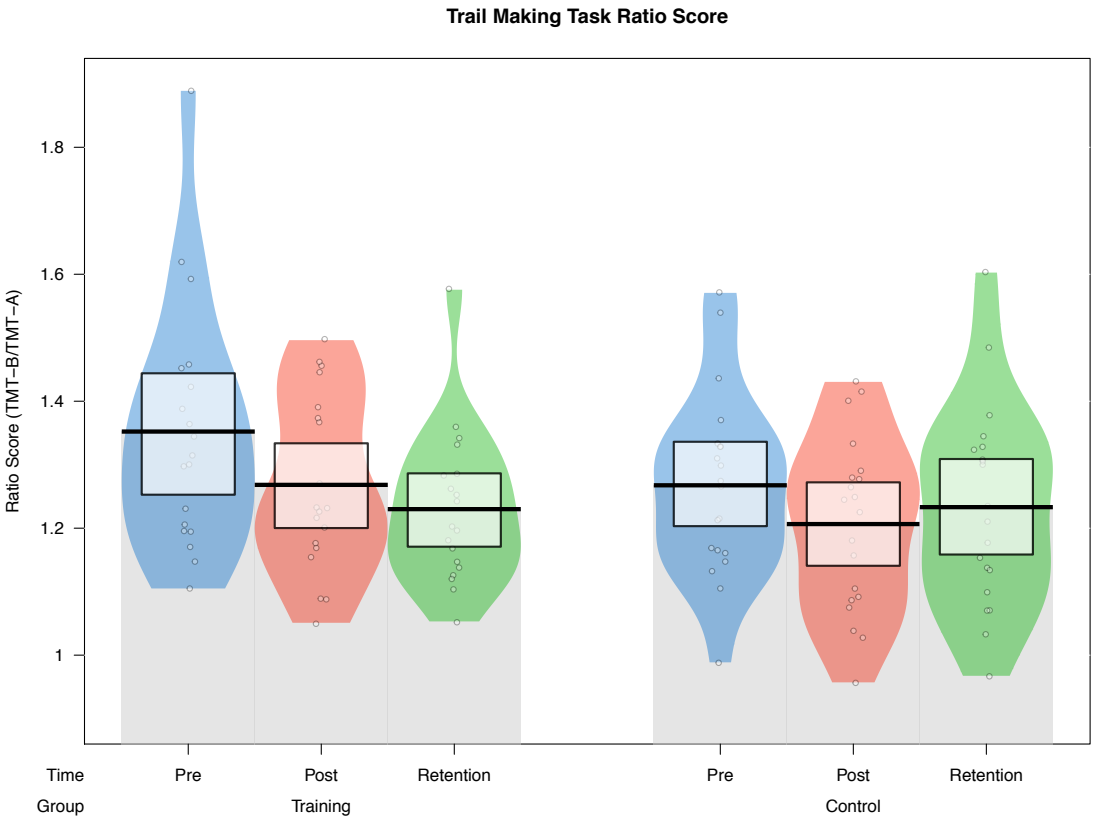

Figure 2.5-10 Pirate Plot showing the change in the B/A ratio scores across Session for Training and Control Groups. The training group retention session 95% HDI falls largely below the pre-test ratio score interval, suggesting improved performance. No reliable differences can be observed across session for the control group.

2.5.7 Sustained Attention to Response Task (SART)

Two outcome variables for the SART were analysed, 'commission errors' and 'omission errors'. Commission errors are incorrect responses to 'NO-GO' trials, i.e. incorrectly pressing the mouse button in response to the number 3 stimulus. Omission errors are a failure to respond to 'GO' trials, i.e. failing to click the mouse button in response to numbers 1-2, 4-9. Both types of error purportedly reflect lapsing attention by indicating a break in task engagement. Commission errors are also said to reflect inhibitory control function, as participants have to withhold the automatic response (Manly, Robertson, Galloway & Hawkins, 1999).

Model:

For both outcome variables, the MCMCglmm model included Time as a designated fixed effect, and Gender was included as a covariate. Participants crossed

with Time (levels = pre, post, retention) was included as a random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's *f*) were calculated.

2.5.7.1 Omission Errors

Data Cleaning:

One outlier was identified, using the adjusted boxplot method, as falling above the upper extreme fence (35.5 errors). This value was a pre-test value originating from the control group, and was removed prior to analysis.

Analysis:

Planned contrasts using pairwise comparisons to look at differences in Omission Errors across sessions revealed the number of Omission errors to be lower for the training group post-intervention, and this was designated a large effect (p=0.001, Cohen's f= 0.56). No changes in Omission error scores were found in the control group across pre-post or pre-retention contrasts.

Table 2.5-10: Mean Omission Error Scores, Pre-Post and Pre-Retention Session Contrasts.

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	6.34 (1.39)	1.93 (1.40)	2.98 (1.39)	**0.001***	**0.56**	38	**0.007***	0.22	38
Control	6.02 (2.03)	3.71 (1.98)	3.85 (2.04	0.136	0.27	30	0.174	0.12	30

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

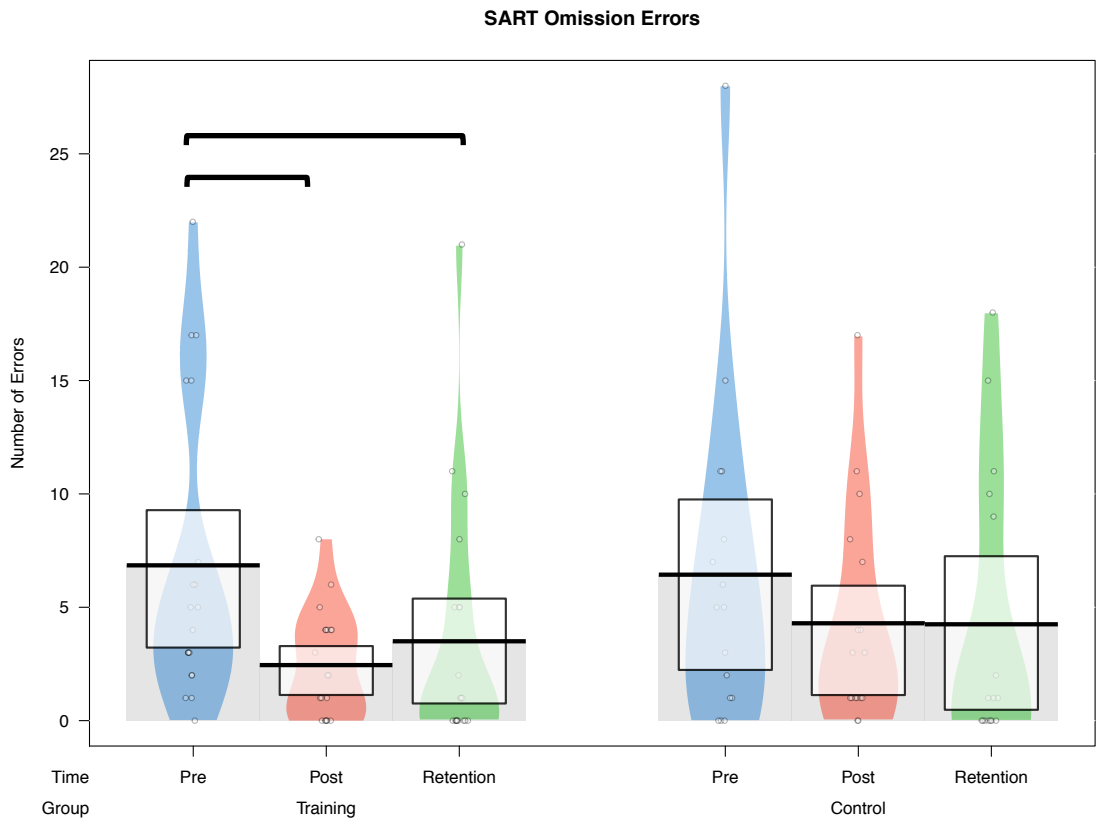

Figure 2.5-11 Pirate plot indicating numbers of omission errors made across sessions for the training and control groups. For the training group, the 95% HDI at the post-test falls below the interval for the pre-test session, indicating a high probability that Error scores were reliably lower post-intervention. In the control group post session, the 95% HDI falls largely within the pre-test interval, indicating no reliable difference was observed. .

2.5.7.2 Commission Errors

Data Cleaning:

No outliers were identified by adjusted boxplots.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups found the number of commission errors was lower for both the training group ($p<0.000$, Cohen's $f= 0.78$) and the control group ($p=0.000$, Cohen's $f= 0.72$) post-intervention, and these were designated large effects. Similarly, scores remained markedly lower at the retention session for both the training group ($p<0.000$, Cohen's $f= 0.35$) and controls ($p<0.000$, Cohen's $f= 0.32$), however only a medium effect size was observed at retention.

Table 2.5-11 Mean Commission Error Scores, and Pre-Post and Pre-Retention Session Contrasts.

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	2.35 (0.35)	0.75 (0.36)	0.89 (0.35)	**0.000***	**0.78**	38	**0.000***	**0.35**	38
Control	2.54 (0.69)	0.84 (0.69)	1.01 (0.71)	**0.000***	**0.72**	31	**0.001***	**0.31**	31

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

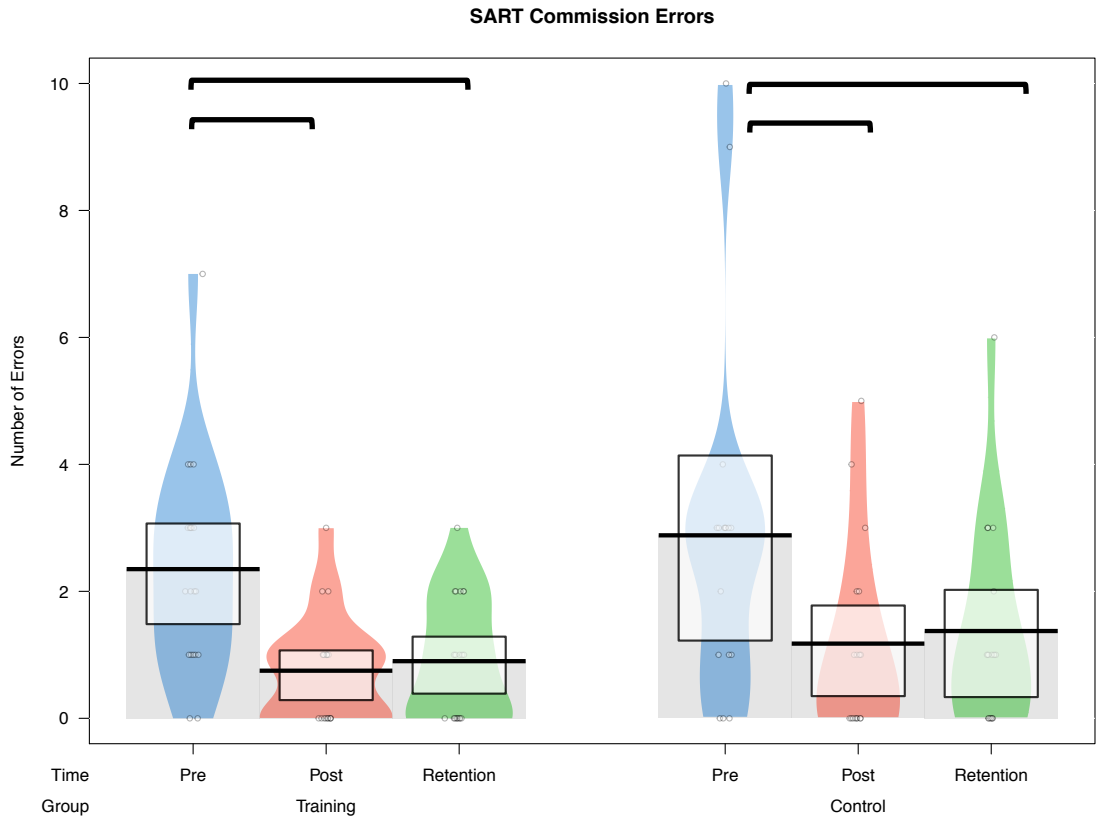

Figure 2.5-12 Pirate plot indicating numbers of commission errors made across sessions for the training and control groups. For the training group, the 95% HDI at the post-test falls below the interval for the pre-test session, indicating a high probability that Error scores were reliably lower post-intervention. In the control group post session, the 95% HDI falls reliably below the pre-test interval, also indicating that reliable difference were observed. Retention test scores were also reliably lower than pre-test scores across both training and control groups.

2.5.8 Grip Strength and Dexterity

Grip Strength: No differences in grip strength were observed between the pre-test session and the post-test or retention-test session for either the motor training group or the active control group.

Dexterity: No differences in dexterity were observed between the pre-test session and the post-test or retention-test session for either the motor training group or the active control group.

2.5.8.1 Experiment 1: Summary

Table 2.5-12 Experiment 1: Cognitive Results Summary Table

	Training							Control						
Cognitive Test	**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**		**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**	
	Pre	**Post**	**Retention**	**P**	***f***	**p**	***f***	**Pre**	**Post**	**Retention**	**p**	***f***	**p**	***f***
Flanker														
Conflict Cost	30.9 (11.1)	21 (10.9)	28.6 (10.9)	0.462	0.12	0.862	0.01	40.5 (10.3)	36.4 (10.5)	47.7 (9.9)	0.741	0.06	0.547	0.05
CRT														
Cognitive RT	487(26)	439(26)	443(26)	**.000***	**0.41**	0.002*	0.18	489(37)	481(37)	471(37)	0.483	0.08	0.119	0.09
Motor RT	374(21.5)	337(21.6)	342(21.8)	**0.018***	**0.27**	0.045*	0.11	362(39.7)	336(39.5)	319(39.7)	0.254	0.14	0.055	0.11
Vis n-Back														
Vis Accuracy														
1-back	.902 (.066)	.973 (.065)	.974 (.065)	0.191	0.38	0.190	0.37	.967 (.068)	.983 (.067)	.988 (.069)	0.800	0.12	0.734	0.08
2-back	.627 (.066)	.657 (.066)	.784 (.066)	0.589	0.08	0.004*	0.19	.585 (.069)	.739 (.068)	.742 (.069)	**0.013***	**0.32**	0.012*	0.16
Visual RT														
1-back	642(75.8)	575(76.8)	583(76.4)	0.394	0.28	0.458	0.12	592(82)	614(83.5)	618(83)	0.813	0.09	0.783	0.05
2-back	846(76.6)	721(77.2)	794(77)	0.111	0.25	0.510	0.05	752(85.8)	886(82.2)	733(82.9)	0.161	0.36	0.842	0.02
TMT														
Ratio B/A	1.35 (.05)	1.31 (.050)	1.28 (.049)	0.460	0.08	0.174	0.07	1.25 (.052)	1.23 (.052)	1.23 (.051)	0.715	0.03	0.717	0.02

Table 2.5-12 Experiment 1: Cognitive Results Summary Table (*continued*).

	Training							Control						
Cognitive Test	**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**		**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**	
Dual n-Back	**Pre**	**Post**	**Retention**	**P**	***f***	**p**	***f***	**Pre**	**Post**	**Retention**	**p**	***f***	**p**	***f***
Vis Accuracy														
1-back	.693 (.065)	.789 (.065)	.852 (.066)	0.079	0.33	**0.003***	**0.28**	.745 (.068)	.892 (.068)	.869 (.068)	**0.017***	**0.39**	0.042*	0.17
2-back	.289 (.069)	.389 (.072)	.485 (.072)	0.103	0.30	**0.002***	**0.26**	.358 (.068)	.405 (.068)	.466 (.069)	0.448	0.16	0.083*	0.15
Aud Accuracy														
1-back	.825 (.073)	.905 (.073)	.899 (.073)	0.233	0.34	0.278	0.16	.887 (.062)	.906 (.062)	.892 (.061)	0.582	0.11	0.770	0.03
2-back	.464 (.078)	.461 (.077)	.544 (.076)	0.968	0.02	0.267	0.06	.436 (.062)	.566 (.06)	.569 (.06)	**0.017***	**0.35**	0.014*	0.17
Visual RT														
1-back	1384(75.2)	1285(76.5)	1180(76.6)	0.207	0.23	0.009*	0.24	1286(82.3)	1270(82.4)	1214(83.5)	0.864	0.03	0.440	0.07
2-back	1833(81.1)	1637(84.4)	1654(87.1)	0.026*	0.24	0.050*	0.12	1599(82.9)	1464(84)	1455(85.6)	0.156	0.20	0.133	0.10
Auditory RT														
1-back	1301(103)	1002(103)	1070(104)	**0.009***	**0.43**	0.044*	0.17	1071(97)	1130(96)	1027(97)	0.557	0.11	0.670	0.04
2-back	1483(111)	1551(107)	1518(107)	0.573	0.09	0.773	0.02	1449(97)	1591(97)	1541(99)	0.170	0.20	0.380	0.06
SART Errors														
Omission	6.34 (1.39)	1.93 (1.40)	2.98 (1.39)	**0.001***	**0.56**	0.007*	0.22	6.02 (2.03)	3.71 (1.98)	3.85 (2.04)	0.136	0.27	0.174	0.12
Comission	2.35(0.35)	0.75(0.36)	0.89(0.35)	**0.000**	**0.78**	**0.000**	**0.35**	2.54(0.69)	0.84(0.69)	1.01(0.71)	**0.000**	**0.72**	**0.001**	**0.31**

2.6 Kinematic Results

2.6.1 Summary

Adaptation to the Baseline Motor Task

The motor training gave rise to changes in performance on the baseline motor task, with the training group exhibiting shorter movement times and lower path deviation at the post-test session.

1. **Movement Time:** MT on the baseline motor task was lower for the trained limb for the training group at post and retention sessions.
2. **Path Deviation:** PD on the baseline motor task was lower for the trained limb for the training group at post and retention sessions.

No reliable changes were seen for the training group on measures of heading error or peak velocity. For the control group, no reliable changes were seen on the baseline motor task for any movement characteristics at the post-intervention or retention test sessions.

Association between adaptation to the motor task, and performance in cognitive measures

To establish whether there were relationships between the measures of adaptation derived for the individual participants to the baseline motor task, and the degree of improvement exhibited by individuals on the tests of cognitive function, statistical measures of association were calculated for assessments of cognitive function for which reliable changes from pre- to post-intervention had been obtained. However, no associations were seen between change in individual adaptation to the motor task and change in individual cognitive performance.

2.6.2 Data Processing and Analysis

Movement time series data were digitally filtered (second order, dual-pass Butterworth filter, low-pass 6 Hz) and the transducer derived displacement recordings for the two orthogonal degrees of freedom (flexion; extension; radial deviation; ulnar deviation) were defined in sensor space. To determine movement onset time, we applied

a variant of the algorithm defined by Teasdale et al., (1993), to a derived time series where all samples were expressed as a displacement from the origin of the task space.

Reaction time (RT) was calculated as the period of time elapsing between initial target appearance and movement onset. RTs under 200ms were interpreted as anticipation of target presentation, and thus were removed from further analysis. Movement time (MT) was calculated as the period of time that elapsed between movement onset time and target acquisition. The derived displacement time series was differentiated to obtain the rate of change of velocity, and the maximum value of this measure (peak velocity) was established for the interval between movement onset and target acquisition. The time at which peak velocity occurred was also recorded.

Path deviation was utilised as a measure of the spatial characteristics of movement trajectory between movement onset and target acquisition. The difference between points on the movement time series trajectory and the straight-line trajectory between starting position and the target was calculated for all samples in the interval between movement onset and the initial encounter with the target zone (within 10% of the target radius). The sum of root mean squared (r.m.s) of all values in the interval, the r.m.s. path deviation, was then calculated. This measure indicated the overall magnitude of deviance from the straight-line trajectory between movement onset position and target.

The smoothness of the movement trajectory for the interval between movement onset and the initial encounter with the target zone was defined as the spectral arc length (SAL), a dimensionless measure independent of amplitude and duration (Balasubramanian et al., 2012, 2015). SAL has previously been validated as a sensitive, reliable and practical measure of smoothness, which overcomes difficulties associated with using measures based on jerk (Balasubramanian et al., 2015).

Heading deviation, the difference between desired heading and actual heading, was calculated in a 10ms window centred 100ms following movement onset. Heading deviation was taken as a measure of the efficiency of *feedforward* processes, as it was assumed that adjustments of movement trajectory facilitated by visual feedback of the cursor were not possible prior to 100ms. For each sample in this interval, the angle between two spatial vectors was calculated: the vector from the point at movement onset to the target position, and the vector from the point at movement onset to the point at the movement time series for that sample. Circular statistical methods were then used to calculate the mean direction of the angles in the 10ms interval centred at 100ms. To ensure heading deviation measures only included trajectories characterised as initial impulses away from the starting position, cases were removed if cursor velocity failed to

display an increasing trend (assessed using Sen's Slope) during the initial 100ms movement interval. Beyond this exception, heading deviation was calculated for all trials. Heading error at 100ms was obtained for all trials, whereas the remaining measures (MT, peak velocity, r.m.s. path deviation and SAL) were derived only for trials on which the target was acquired,

2.6.3 Statistical Analysis

All statistical analyse were carried out using R statistical software (R Core Team, 2012). A Bayesian re-sampling approach was employed to reduce the effective degree of autocorrelation and deal with violations of normality (i.e. of the residuals) so that transformation of the dependent variable was not necessary. Weakly informative inverse Wishart priors were used for the random and fixed effects. All analyses were set at 13,000 iterations, and the thinning interval was set at 10, with a burn-in of 3,000. Diagnostic checks for convergence were carried out on all analyses. The resulting effective sample size was 100 for each parameter.

Model:

For all movement characteristics, the MCMCglmm model included Time (levels = pre, post, retention) crossed with Limb (levels= Left, Right), Block (levels= 1, 2, 3, 4), and Target (levels = flexion, flexion-radial, radial, extension-radial, extension, extension-ulnar, ulnar, flexion-ulnar) was a designated fixed effect. Participants crossed with Limb, Time and Target were included as random effects.

Planned Contrasts:

For each of the movement characteristics outlined above, least square means obtained prior to the intervention (pre), following the intervention (post) and at a retention session following a period of no training (ret) were compared, and planned contrasts were carried out on the mean differences using pairwise comparisons. Separate analyses were carried out for the intervention (Motor Training) and active control (Control) groups.

All contrasts were carried out between the fourth block of the baseline task on day one, and the first block of the baseline task at the subsequent post-test and retention-test sessions. This was in effort to avoid inadvertently biasing the pre-test scores, as early adaptation to the task would occur rapidly over the initial blocks of the task at the pre-test session. In order to ‘wash-out’ these effects and exclude them from analysis, only the fourth block of the baseline task was included.

In addition to examining the left (trained) limb, the performance of the right, untrained limb was also considered. The objective was to assess the generality of the adaptations that arose from the five days of training. To effects of this nature – when expressed as changes in the performance of the untrained limb, the terms “cross education” and “interlimb transfer” have been applied.

2.6.4 Movement Time: Baseline Visuomotor Task

Movement time (MT) was calculated as the period that elapsed from movement onset to target acquisition.

2.6.4.1 Motor Training Group

Left (training) limb: Movement Time scores were lower following training than prior to training in the case of two targets, 'radial' and 'flexion-ulnar'. These effects remained present at retention, for both radial and flexion-ulnar targets. Additionally, Movement Time was also lower at the time of the retention test for the 'flexion' target (495ms, $p < 0.023$).

Right (transfer) limb: MT scores at two target locations were lower at post-test sessions compared to pre-test. These were for the 'radial' ($p=0.004$) and extension-radial' ($p=0.037$) targets. However, this difference was not observed at retention, where all MT scores could not reliably be distinguished from pre-test scores.

2.6.4.2 Control Group:

Left limb: For participants carrying out the control intervention, Movement Time scores were not reliably and systematically different from pre-test scores at either the post-test or retention test sessions.

Right limb: MT measures for all targets did not change in a reliable and systematic manner for the right limb contrasts, with one exception: right 'ulnar' target MT was lower at retention ($p=0.026$) than at pre-test.

Movement Time for the Training Group Left Hand

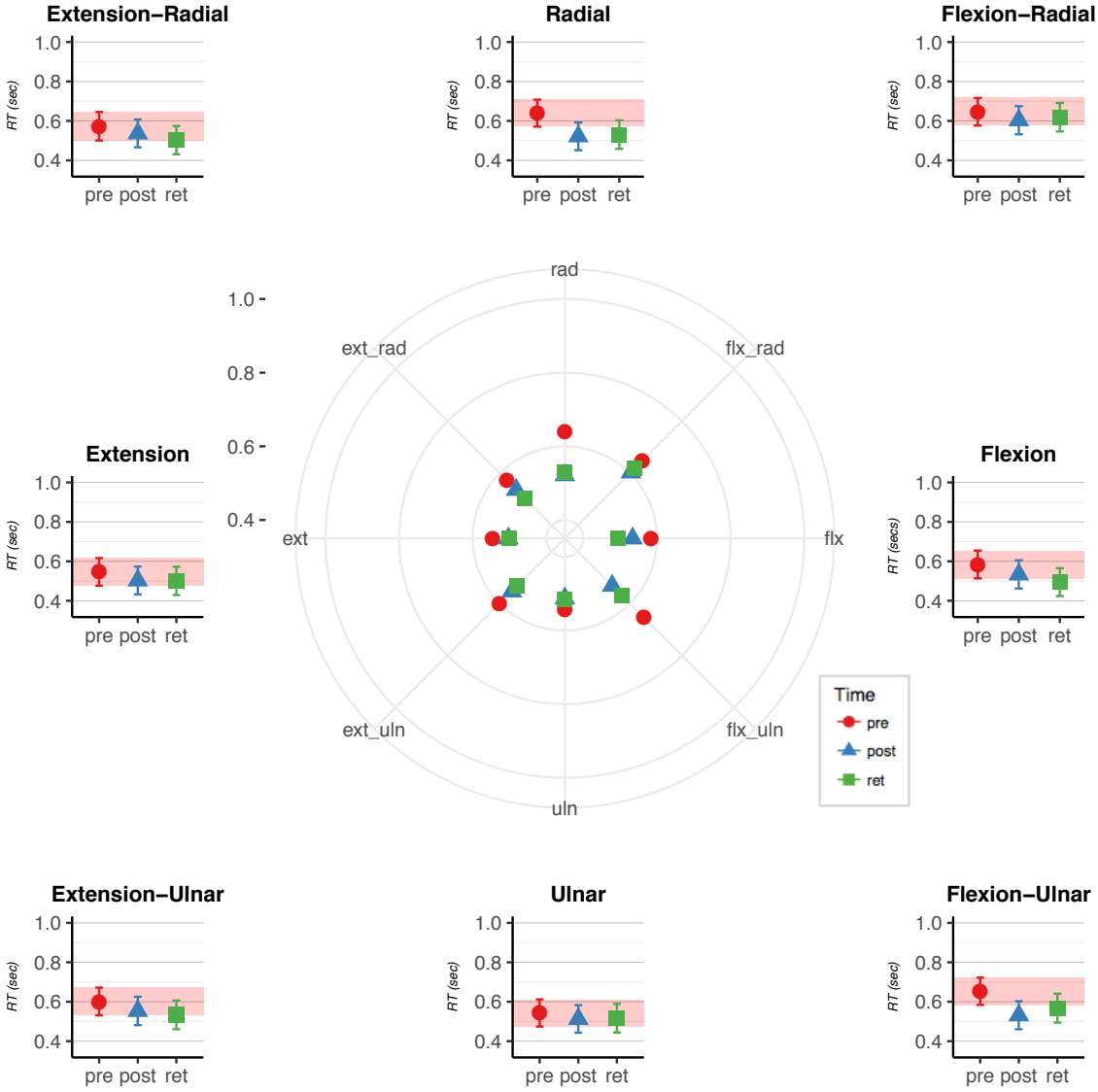

Figure 2.6-1 Changes in LH Movement Time for the Training Group across all anatomical targets. For the 'radial' and 'flexion-ulnar' targets, post-test scores and retention-test scores are lower than at the pre-test session. For the 'flexion' target, retention-test MT is lower than at pre-test. Across all targets, a decrease in MT is observed from pre-test to post-test.

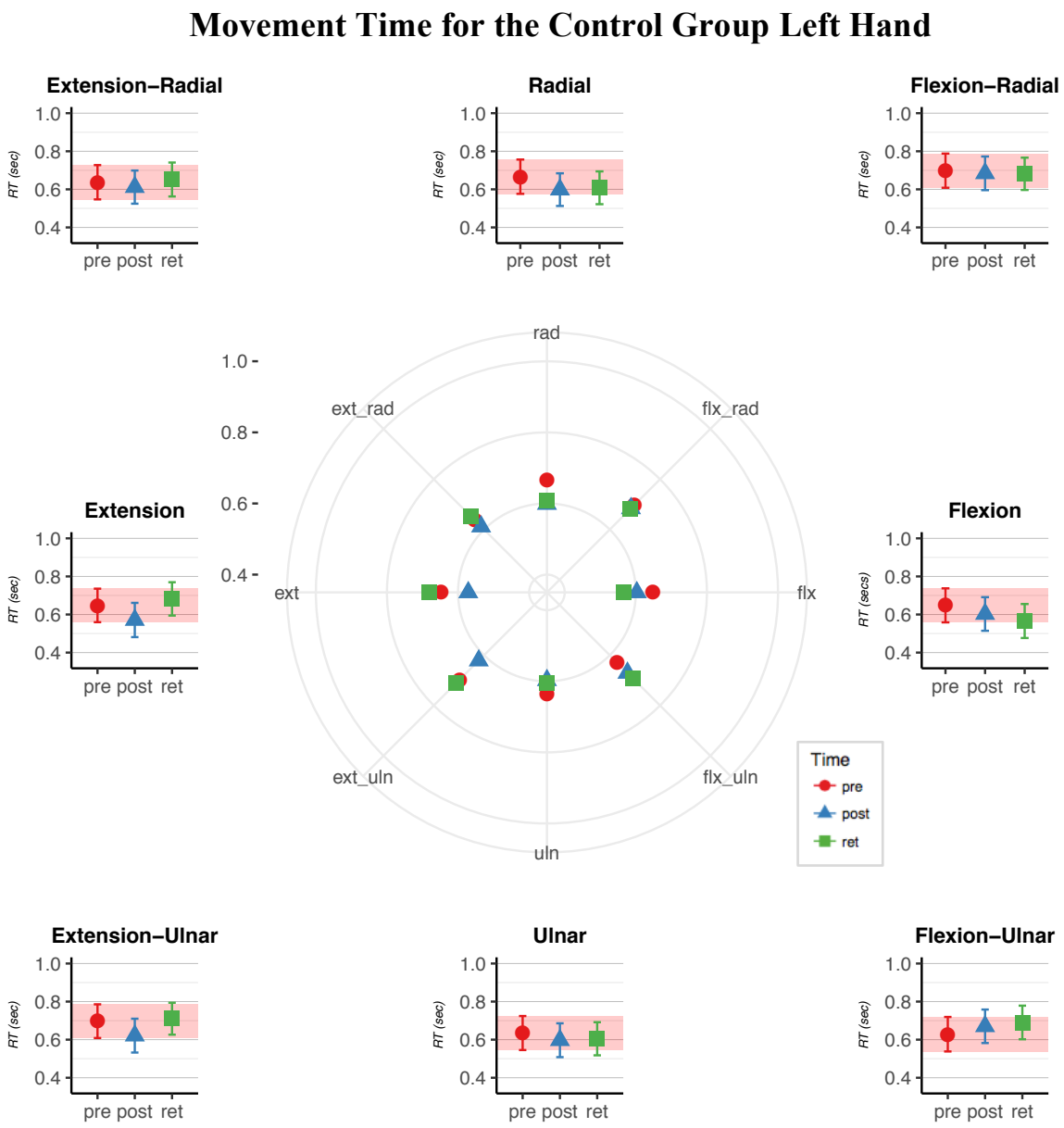

Figure 2.6-2 Changes in LH Movement Time for the Control Group across all anatomical targets. MT post-test and retention-test scores cannot reliably be distinguished from pre-test scores across all target locations, as their means all fall within the 95% confidence intervals for the pre-test score.

Table 2.6-1 Pre–post and pre-retention Movement Time contrasts for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.584	0.534	0.495	0.194	**0.023***	0.648	0.603	0.566	0.320	0.074
	flx_rad	0.647	0.604	0.619	0.257	0.491	0.698	0.684	0.682	0.769	0.728
	rad	0.639	0.522	0.531	**0.002***	**0.006***	0.666	0.599	0.608	0.137	0.187
	ext_rad	0.573	0.537	0.503	0.361	0.075	0.637	0.612	0.652	0.588	0.763
	ext	0.547	0.503	0.501	0.263	0.231	0.648	0.571	0.682	0.095	0.447
	ext_uln	0.601	0.553	0.533	0.203	0.086	0.697	0.621	0.710	0.112	0.775
	uln	0.543	0.513	0.517	0.425	0.494	0.635	0.597	0.605	0.409	0.515
	flx_uln	0.653	0.532	0.568	**0.001***	**0.035***	0.629	0.670	0.690	0.367	0.190

Table 2.6-1 Pre–post and pre-retention Movement Time contrasts for the Training and Control Groups *(continued)*

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.475	0.534	0.498	0.127	0.563	0.598	0.627	0.573	0.550	0.601
	flx_rad	0.587	0.626	0.604	0.335	0.660	0.701	0.687	0.683	0.774	0.715
	rad	0.531	0.645	0.566	**0.004***	0.372	0.587	0.653	0.647	0.163	0.206
	ext_rad	0.561	0.642	0.549	**0.037***	0.772	0.564	0.655	0.631	0.057	0.172
	ext	0.558	0.624	0.520	0.090	0.328	0.566	0.609	0.591	0.383	0.595
	ext_uln	0.573	0.639	0.557	0.099	0.678	0.576	0.667	0.652	0.051	0.113
	uln	0.571	0.645	0.559	0.053	0.746	0.714	0.663	0.607	0.272	**0.026***
	flx_uln	0.512	0.585	0.518	0.063	0.878	0.650	0.677	0.636	0.562	0.780

2.6.5 Intervention Group Movement Time: Visuomotor Training Task

For the intervention training group, mean Movement Time increased over the course of the training days as task difficulty increased.

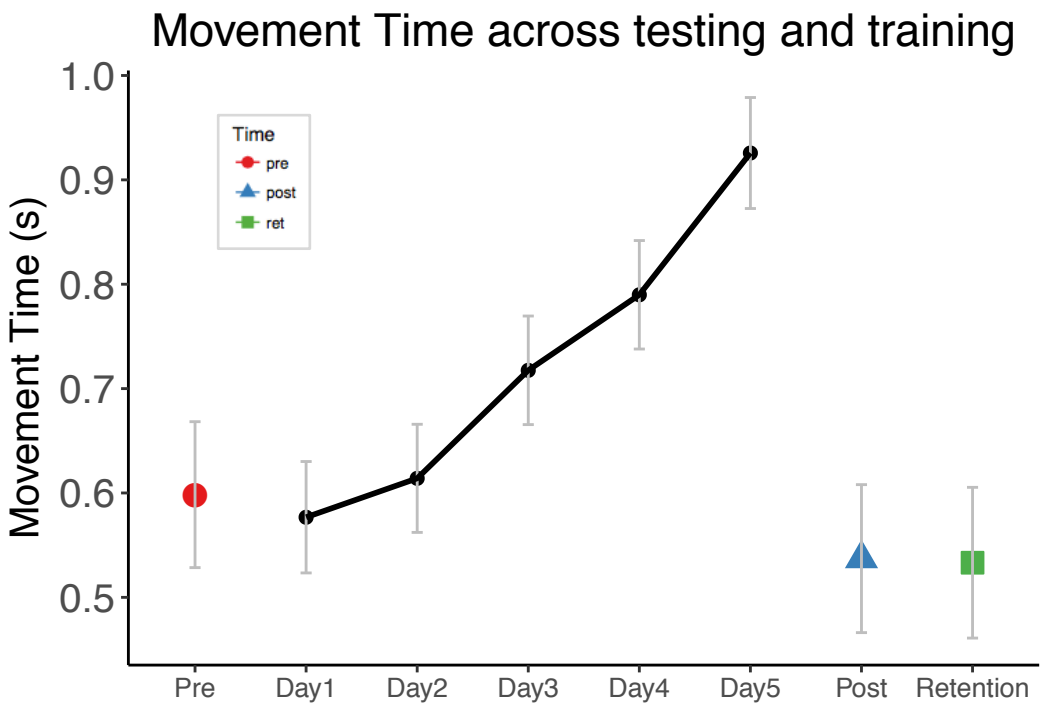

Figure 2.6-3 Changes in intervention group Movement Time across testing sessions and training days. The average MT across all targets is shown for each testing session, Pre, Post and Retention. In addition, the average MT across training day is shown in the centre of the figure, connected with a black line. Mean movement time on the visuomotor training task increased across training days as the task difficulty increased. Post-test and retention-test overall mean MTs (across all target locations) are lower than mean MT at the pre-test session.

Table 2.6-2 Mean Movement Time values by Training Day, and contrasts with Day 1 mean MT.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	0.577 (0.027)	0.523, 0.630	-
Day 2	0.614 (0.026)	0.562, 0.666	0.082
Day 3	0.718 (0.027)	0.666, 0.770	**0.000***
Day 4	0.790 (0.027)	0.738, 0.842	**0.000***
Day 5	0.926 (0.027)	0.873, 0.979	**0.000***

* indicates $p<0.05$

2.6.6 Spectral Arc Length: Baseline Visuomotor Task

Spectral Arc Length (SAL) is the smoothness of the movement trajectory for the interval between movement onset and initial contact with the Target zone (the area within 10% of the target radius). SAL values that are further from zero indicate 'less smooth' movement trajectories.

2.6.6.1 Motor Training Group

Left (training) limb: Measures of SAL were not reliably different following training at the pre-test or retention-test sessions in comparison to pre-test measures.

Right (transfer) limb: Measures of SAL for four targets were lower (more negative) at post-test sessions compared to pre-test. These were for the 'flexion-radial' ($p=0.025$), 'extension' ($p<0.000$), 'extension-ulnar' ($p=0.005$) and 'ulnar' ($p=0.008$) targets. However, this difference was only observed at retention for the 'flexion-radial' target ($p=0.016$), and in addition, at retention SAL was lower than at the pre-session for the 'radial' target.

2.6.6.2 Control Group:

Left limb: For participants carrying out the control intervention, one target, 'flexion-radial', had a lower (more negative) SAL measure at the post-test than at the pre-test session ($p=0.008$), indicative of 'less smooth' movement trajectories. At the retention session, one target, 'flexion-ulnar', had a lower (more negative) SAL measure than at the pre-test session ($p=0.008$). All other SAL measures were not reliably or systematically different from pre-test scores at either the post-test or retention test sessions.

Right limb: SAL measures for all targets did not change in a reliable and systematic manner for the right limb contrasts, with one exception: right 'extension-radial' target SAL was lower at post-test ($p=0.011$) and at retention ($p=0.026$) than at pre-test.

Spectral Arc Length for the Training Group Left Hand

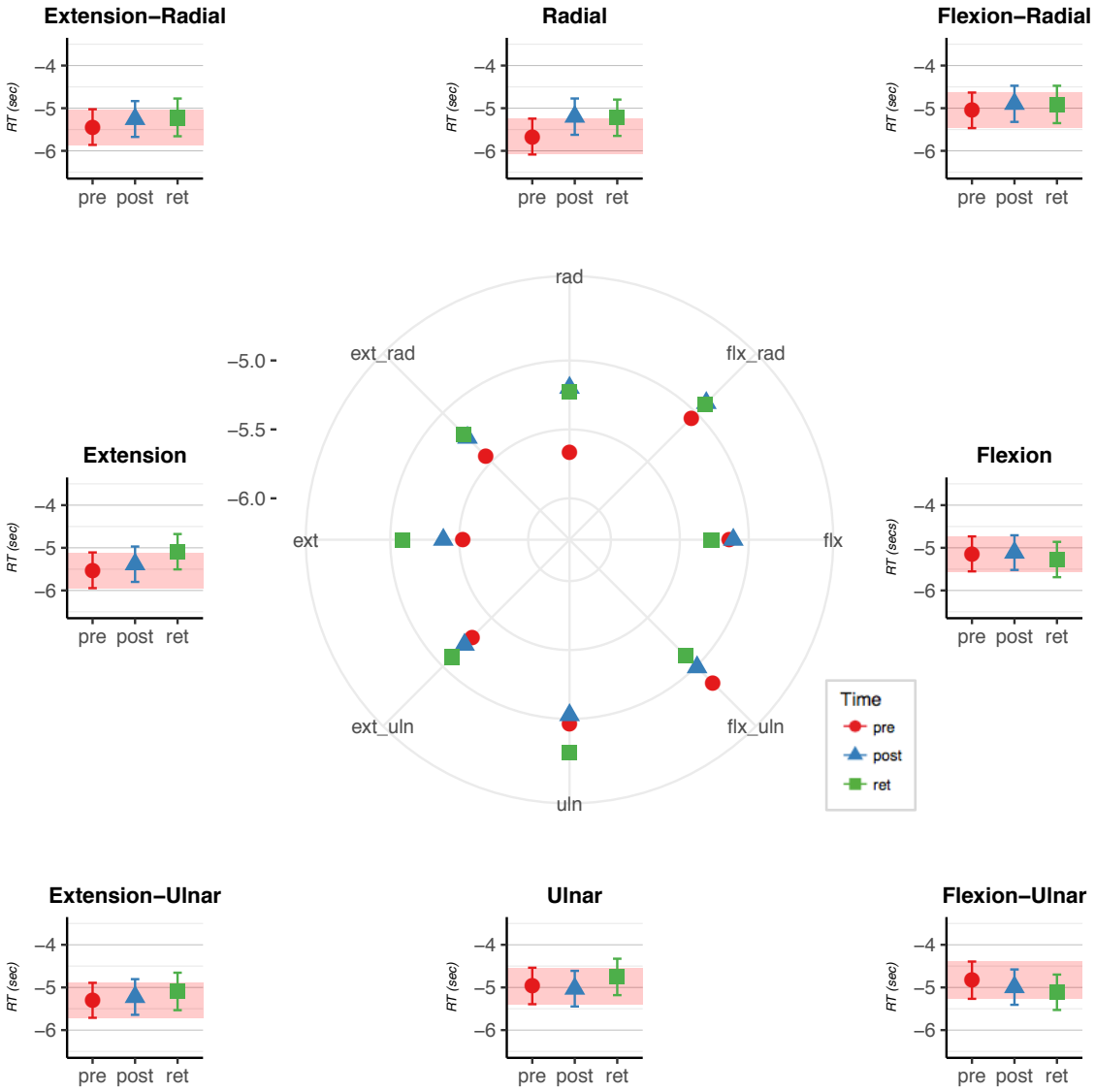

Figure 2.6-4 Training Group differences in SAL for the left hand across Sessions. Measures of SAL were not reliably different following training at the post-test or retention-test sessions in comparison to pre-test measures.

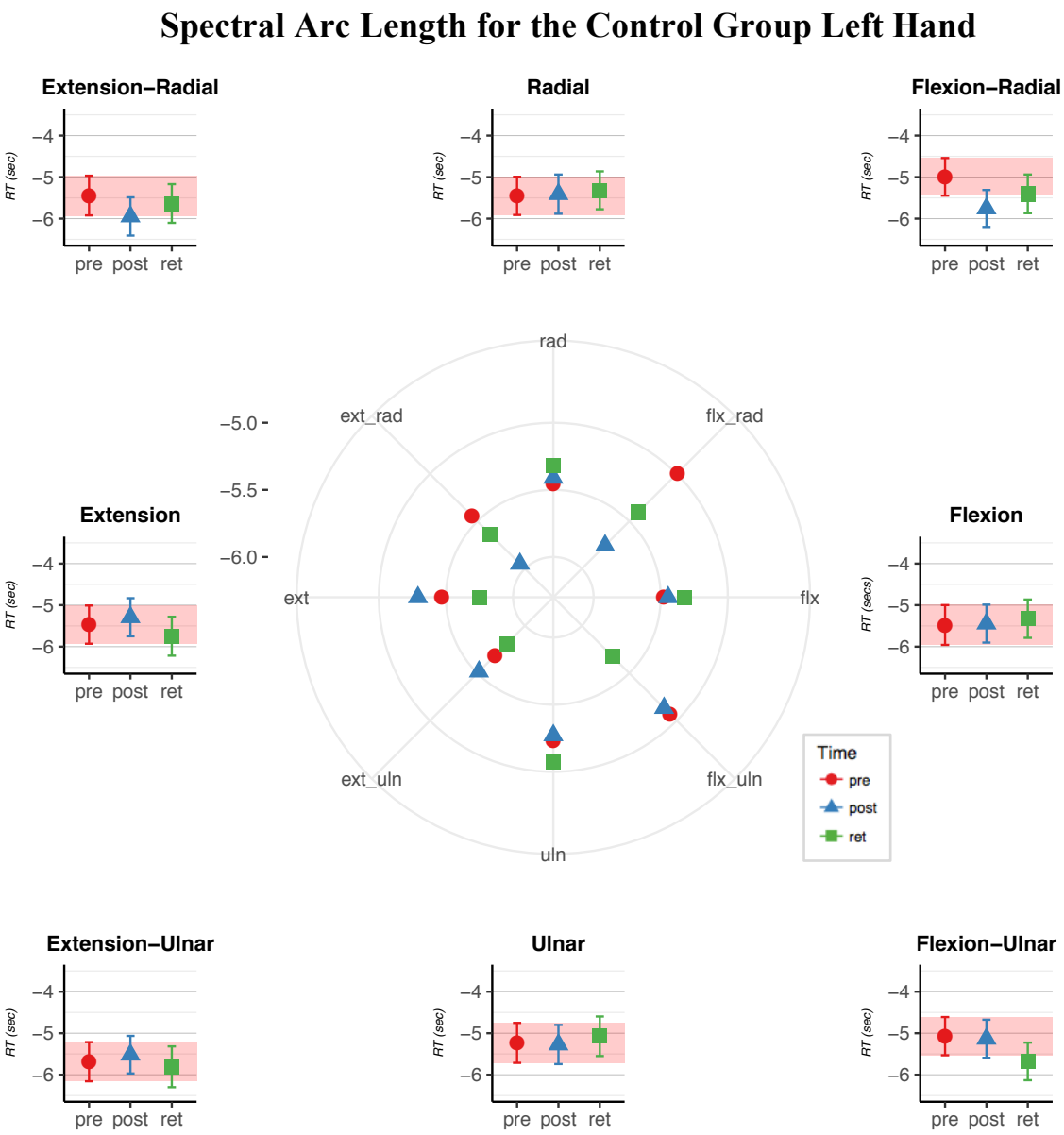

Figure 2.6-5 Control Group differences in SAL for the left hand across testing sessions. The 'flexion-radial' target has a lower SAL measure at the post-test than at the pre-test session. The 'flexion-ulnar' target has a lower SAL measure at retention than at the pre-test session. SAL values that are further from zero (i.e. are more negative) indicate 'less smooth' movement trajectories. All other SAL measures cannot reliably be distinguished from pre-test scores at either the post-test or retention test sessions.

Table 2.6-3 Pre-post and pre-retention contrasts for SAL: Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	-5.142	-5.113	-5.274	0.911	0.639	-5.478	-5.445	-5.326	0.909	0.601
	flx_rad	-5.050	-4.898	-4.912	0.578	0.634	-4.993	-5.755	-5.403	**0.008***	0.146
	rad	-5.665	-5.198	-5.224	0.096	0.112	-5.452	-5.410	-5.318	0.882	0.642
	ext_rad	-5.443	-5.253	-5.216	0.498	0.433	-5.444	-5.948	-5.636	0.096	0.515
	ext	-5.527	-5.385	-5.091	0.600	0.118	-5.469	-5.292	-5.748	0.537	0.345
	ext_uln	-5.301	-5.223	-5.093	0.779	0.453	-5.686	-5.517	-5.808	0.545	0.687
	uln	-4.965	-5.028	-4.753	0.825	0.438	-5.232	-5.272	-5.073	0.894	0.591
	flx_uln	-4.830	-4.992	-5.113	0.577	0.310	-5.070	-5.133	-5.678	0.828	**0.031***

Table 2.6-3 Pre-post and pre-retention contrasts for SAL: Training and Control Groups *(continued)*

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	-4.892	-5.339	-5.332	0.124	0.118	-5.371	-5.659	-5.823	0.348	0.132
	flx_rad	-4.665	-5.299	-5.345	**0.025***	**0.016***	-5.152	-5.474	-5.116	0.282	0.904
	rad	-4.807	-5.335	-5.373	0.058	**0.041***	-5.217	-5.691	-5.578	0.117	0.241
	ext_rad	-5.567	-6.094	-5.688	0.059	0.666	-5.459	-6.192	-6.078	**0.011***	**0.036***
	ext	-5.650	-6.942	-6.109	**0.000***	0.090	-5.824	-5.982	-5.687	0.614	0.645
	ext_uln	-5.610	-6.392	-6.134	**0.005***	0.059	-5.615	-5.858	-5.645	0.419	0.920
	uln	-5.127	-5.900	-5.323	**0.008***	0.483	-5.428	-5.513	-5.292	0.782	0.660
	flx_uln	-4.866	-5.260	-5.257	0.170	0.175	-5.109	-5.530	-5.251	0.162	0.638

2.6.7 Intervention Group Spectral Arc Length: Visuomotor Training Task

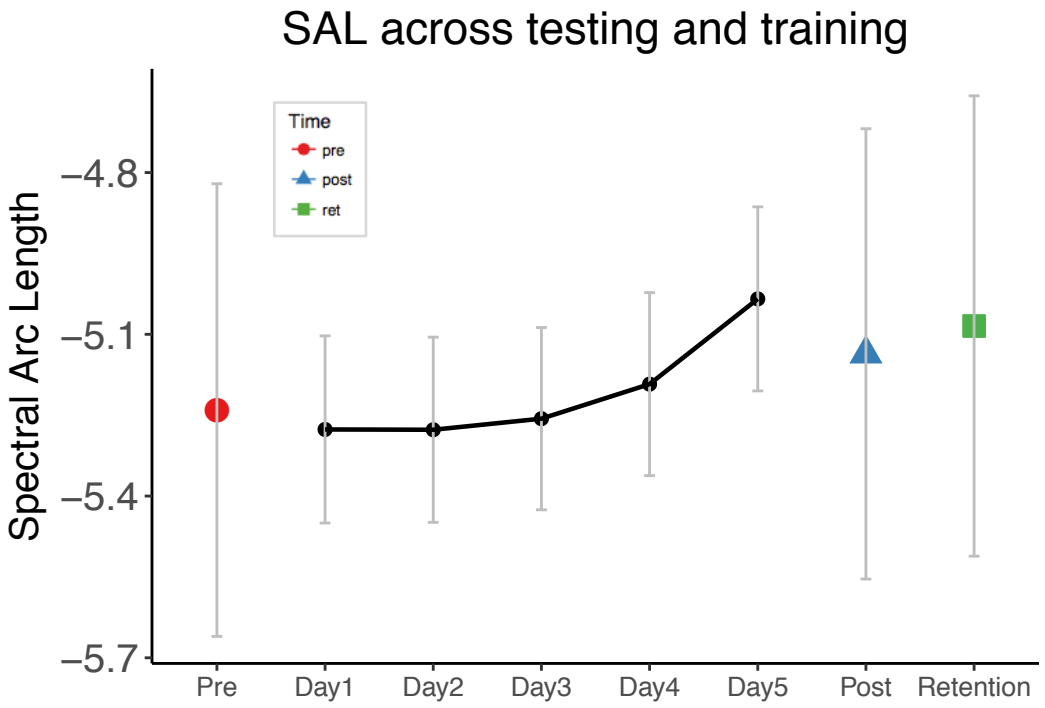

Figure 2.6.7 Changes in Intervention Group Spectral Arc Length across Testing Sessions and Training Days. The average SAL across all targets is shown for each testing session, Pre, Post and Retention. In addition, the average SAL across training day is shown in the centre of the figure, connected with a black line. Mean SAL on the visuomotor training task appears to move in an upward trend from training Day 1 to training Day 5. SAL is slightly less negative at the post-test following training than at pre-test, indicating higher mean smoothness.

Lower mean Spectral Arc Length scores were observed across training days (Table 2.6.4 below). On day 5, SAL scores were systematically lower than on Day 1 ($p<0.001$). SAL measures got 'less negative', indicating smoother movement trajectories between the onset of movement and initial contact with the target zone.

Table 2.6.4: Mean Spectral Arc Length values by Day in the Visuomotor Training Task and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	-5.276 (0.089)	-5.450, -5.103	-
Day2	-5.277 (0.088)	-5.449, -5.105	0.995
Day3	-5.256 (0.086)	-5.426, -5.087	0.827
Day4	-5.192 (0.087)	-5.362, -5.023	0.345
Day5	-5.034 (0.087)	-5.205, -4.864	**0.005***

* indicates $p<0.05$

2.6.8 Path Deviation: Baseline Visuomotor Task

Pre-Acquisition Path Deviation (PD) is a measure of the spatial characteristics of movement trajectory between movement onset and initial contact with the Target zone (the area within 10% of the target radius). PD indicates the overall magnitude of deviance from the straight-line trajectory between movement onset position and target.

2.6.8.1 Motor Training Group

Left (training) limb: PD values were lower at post-test than at the pre-test session for four targets: 'radial' (p=0.011), 'extension-radial' (p=0.008), 'extension' (p=0.029) and 'flexion-ulnar' (p=0.003). At the retention session, these differences were seen in three of the targets: 'radial' (p=0.027), 'extension-radial' (p=0.008), and 'extension'(p=0.046), and an additional fourth target in the 'flexion' position (0.046).

Right (transfer) limb: At the post-training session, PD was systematically lower for only one target, 'extension-ulnar' (p=0.020). The other seven post-test values were not reliably Changes in left-different from at PD values at pre-test. For three targets, 'extension', 'extension/ulnar' and 'ulnar', PD was lower at retention than at the pre-test session. The remaining five post-training values could not be discriminated clearly from those obtained prior to training for the transfer limb.

2.6.8.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for either the Left or Right limb. Similarly, no reliable differences were observed between pre-test PD values and retention session PD values.

Path Deviation for the Training Group Left Hand

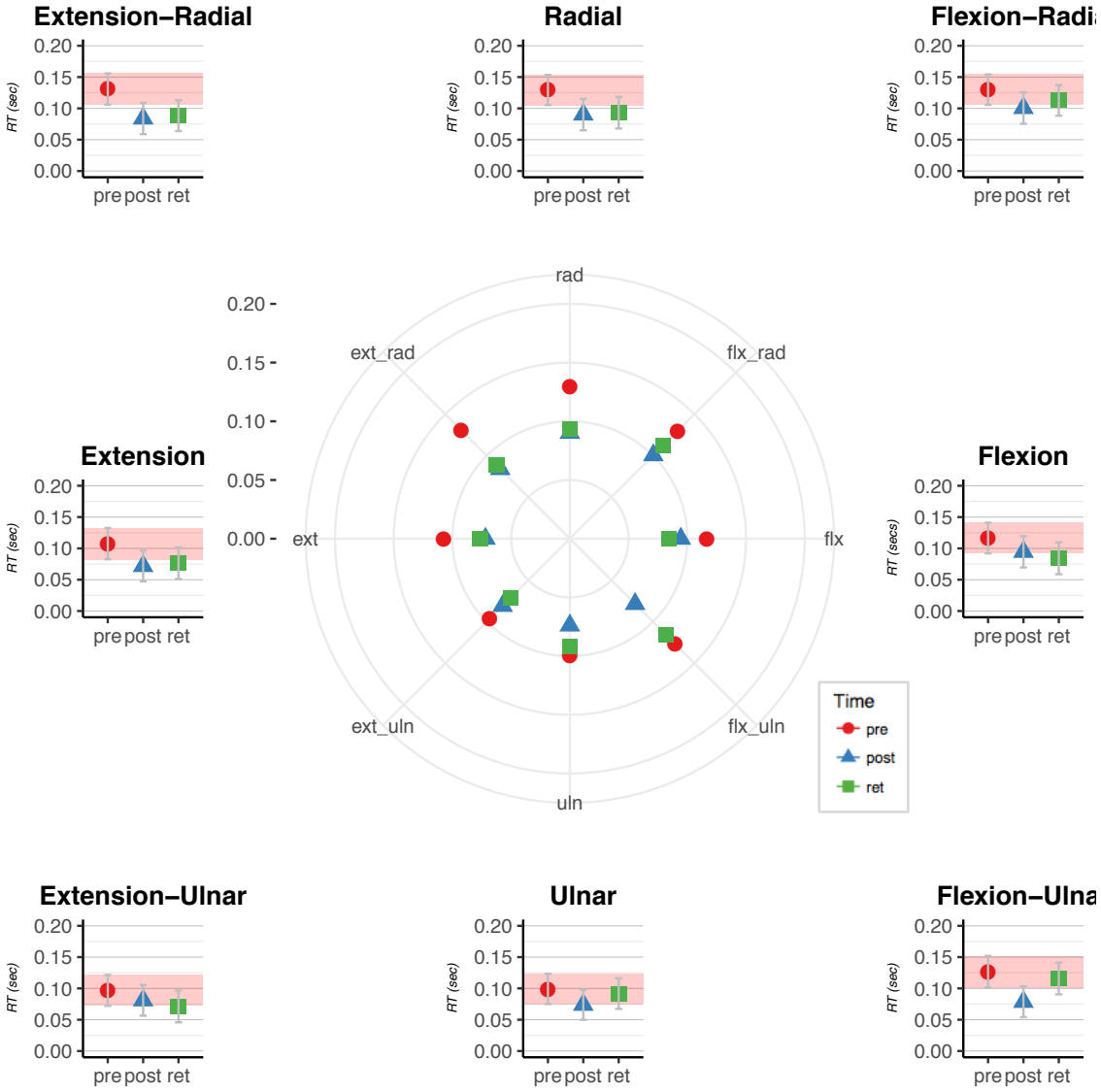

Figure 2.6-7 Changes in left-hand Path Deviation for all targets across sessions for the Training Group. For the targets at extension-radial, radial, extension and flexion-ulnar locations, Path Deviation is lower at post-test than at pre-test. This lower PD score is retained at the retention-test for the extension-radial, radial, and extension targets. In addition, PD for the flexion target is lower at retention.

Path Deviation for the Control Group Left Hand

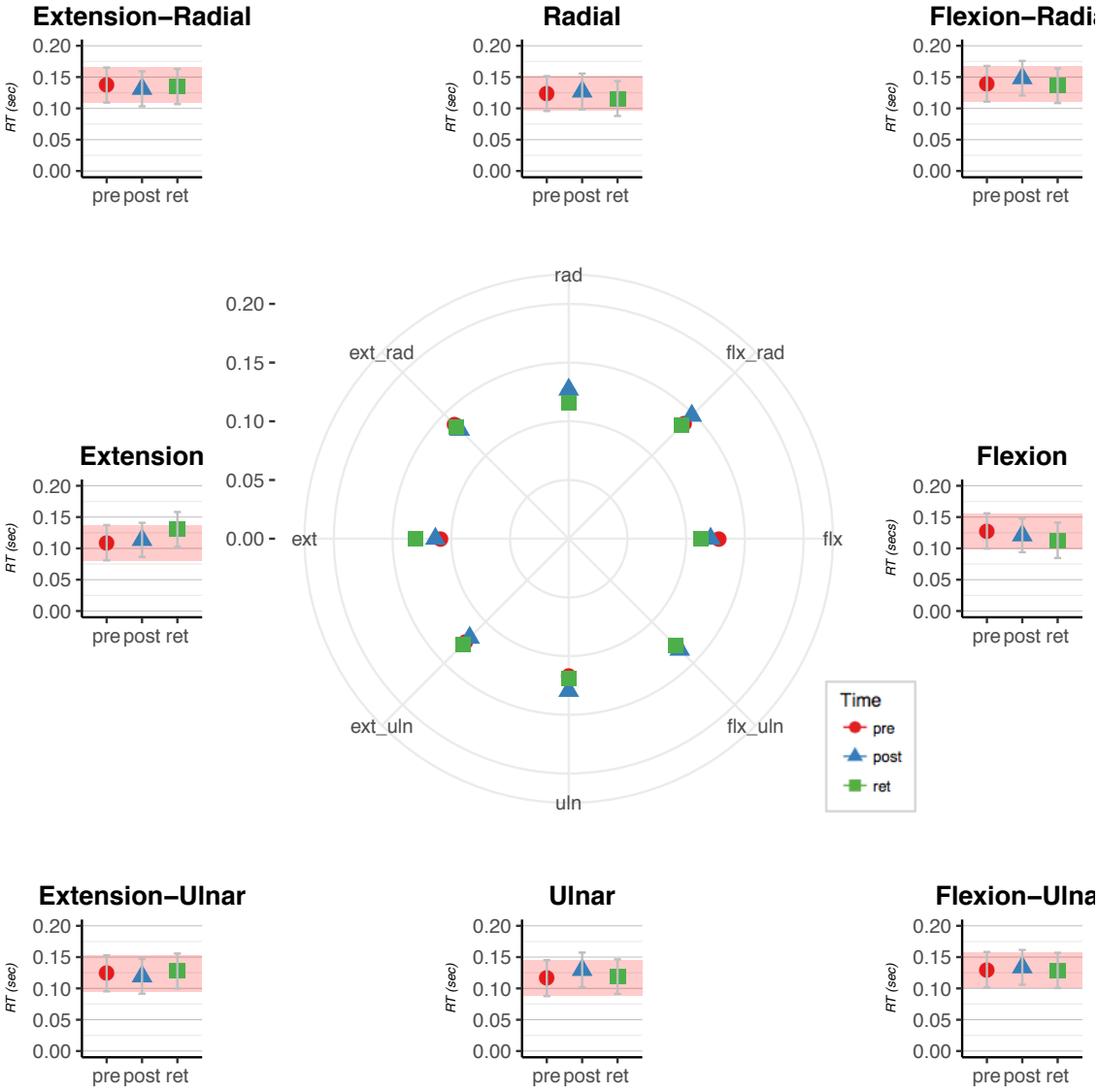

Figure 2.6-8 Changes in left-hand Path Deviation for the Control Group. No reliable differences in Path Deviation can be seen across sessions for any target location, with all post-test and retention-test means falling within the pre-test 95% confidence intervals.

Table 2.6-5 Pre-post and pre-retention contrasts comparing Path Deviation across sessions for Training and Control Groups.

		Training					**Control**				
		Means			**Contrast**		**Means**			**Contrast**	
					Pre-Post	**Pre-Ret**				**Pre-Post**	**Pre-Ret**
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.117	0.094	0.084	0.167	**0.046***	0.128	0.121	0.113	0.639	0.338
	flx_rad	0.130	0.101	0.113	0.056	0.294	0.139	0.148	0.136	0.552	0.843
	rad	0.129	0.090	0.093	**0.011***	**0.027***	0.124	0.127	0.116	0.826	0.586
	ext_rad	0.131	0.084	0.088	**0.004***	**0.008***	0.137	0.131	0.135	0.696	0.877
	ext	0.108	0.072	0.076	**0.029***	**0.046***	0.109	0.114	0.130	0.763	0.152
	ext_uln	0.097	0.081	0.071	0.314	0.118	0.124	0.119	0.128	0.757	0.807
	uln	0.099	0.074	0.092	0.100	0.643	0.116	0.130	0.119	0.377	0.874
	flx_uln	0.127	0.079	0.116	**0.003***	0.522	0.130	0.134	0.129	0.798	0.947

Table 2.6-5 Pre-post and pre-retention contrasts comparing Path Deviation across sessions for Training and Control Groups. (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.086	0.079	0.076	0.660	0.547	0.109	0.091	0.100	0.251	0.558
	flx_rad	0.117	0.103	0.102	0.398	0.348	0.135	0.122	0.116	0.395	0.221
	rad	0.118	0.111	0.106	0.690	0.472	0.123	0.115	0.125	0.593	0.899
	ext_rad	0.113	0.104	0.098	0.579	0.372	0.115	0.101	0.110	0.357	0.736
	ext	0.100	0.076	0.064	0.125	**0.028***	0.084	0.084	0.092	0.964	0.587
	ext_uln	0.110	0.072	0.076	**0.020***	**0.033***	0.100	0.110	0.118	0.521	0.255
	uln	0.114	0.102	0.081	0.456	**0.042***	0.125	0.110	0.116	0.314	0.559
	flx_uln	0.105	0.093	0.077	0.455	0.092	0.112	0.116	0.110	0.783	0.878

2.6.9 Intervention Group Pre-Acquisition Path Deviation: Motor Training Task

Mean Path Deviation scores increased on the motor training task from training Day 1 to training Day 5 ($p<0.000$) as task difficulty increased.

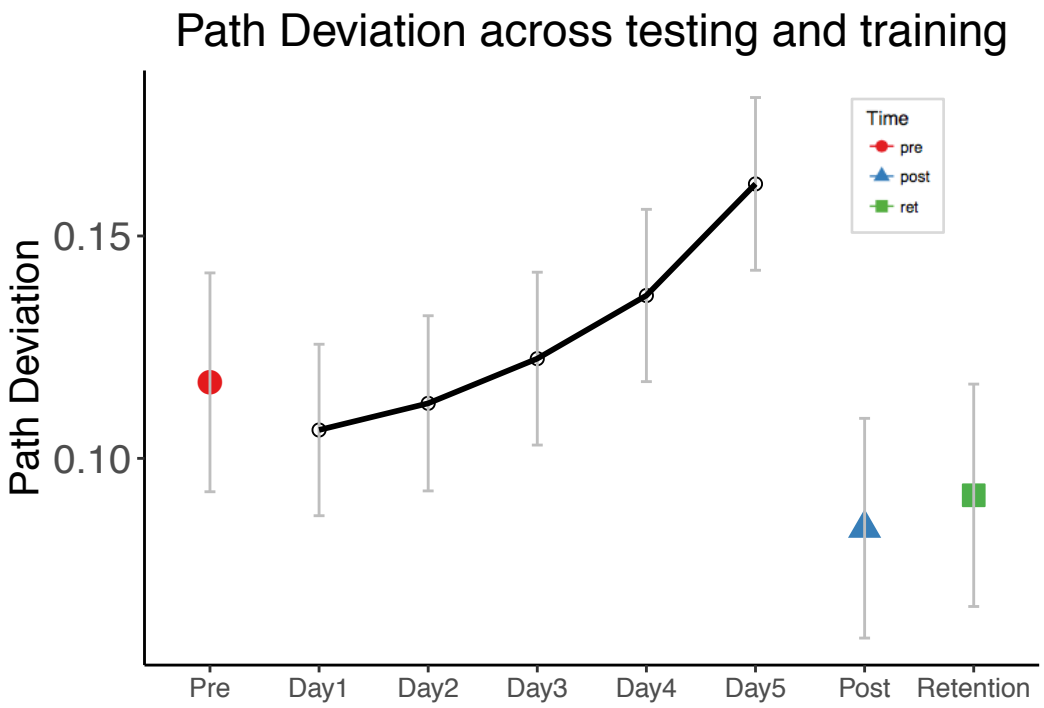

Figure 2.6.9 Changes in Intervention Group Path Deviation across Testing Sessions and Training Days. The average PD across all targets is shown for each testing session, pre, post and retention. In addition, the average PD across training day is shown in the centre of the figure, connected with a blue line. Mean PD on the visuomotor training task appears to move in an upward trend from training Day 1 to training Day 5, indicating greater path deviation with increasing task difficulty. PD is lower at the post-test following training than at pre-test, indicating less path deviation in the movement trajectory, and this decrease in PD is still observed at retention.

Table 2.6-6*:* Mean Path Deviation values by Day in the Visuomotor Training Task, and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	0.106 (.010)	0.087, 0.126	-
Day2	0.112 (.010)	0.093, 0.132	0.519
Day3	0.122 (.010)	0.103, 0.142	0.084
Day4	0.137 (.010)	0.117, 0.156	**0.002***
Day5	0.162 (.010)	0.142, 0.181	**0.000***

* indicates $p<0.05$

2.6.10 Peak Velocity: Baseline Visuomotor Task

Peak Velocity (PV) is the maximum value of the rate of change of velocity for the interval between movement onset and target acquisition.

2.6.10.1 Motor Training Group

Left (training) limb: No systematic differences were observed across all targets at post-intervention or at the retention session for the Left limb.

Right (transfer) limb: At the post-training session, PV was systematically lower for six out of the eight targets. These were the 'flexion', 'radial', 'extension-radial', 'extension', 'extension-ulnar' and 'ulnar' targets. The remaining two post-test target values were not reliably Changes in left-different from PV values at pre-test. At the retention test, only the 'radial' target had lower PD value than at the pre-test.

2.6.10.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for either the Left or Right limb. Similarly, no reliable differences were observed between pre-test PV values and retention session PV values.

Peak Velocity for the Training Group Left Hand

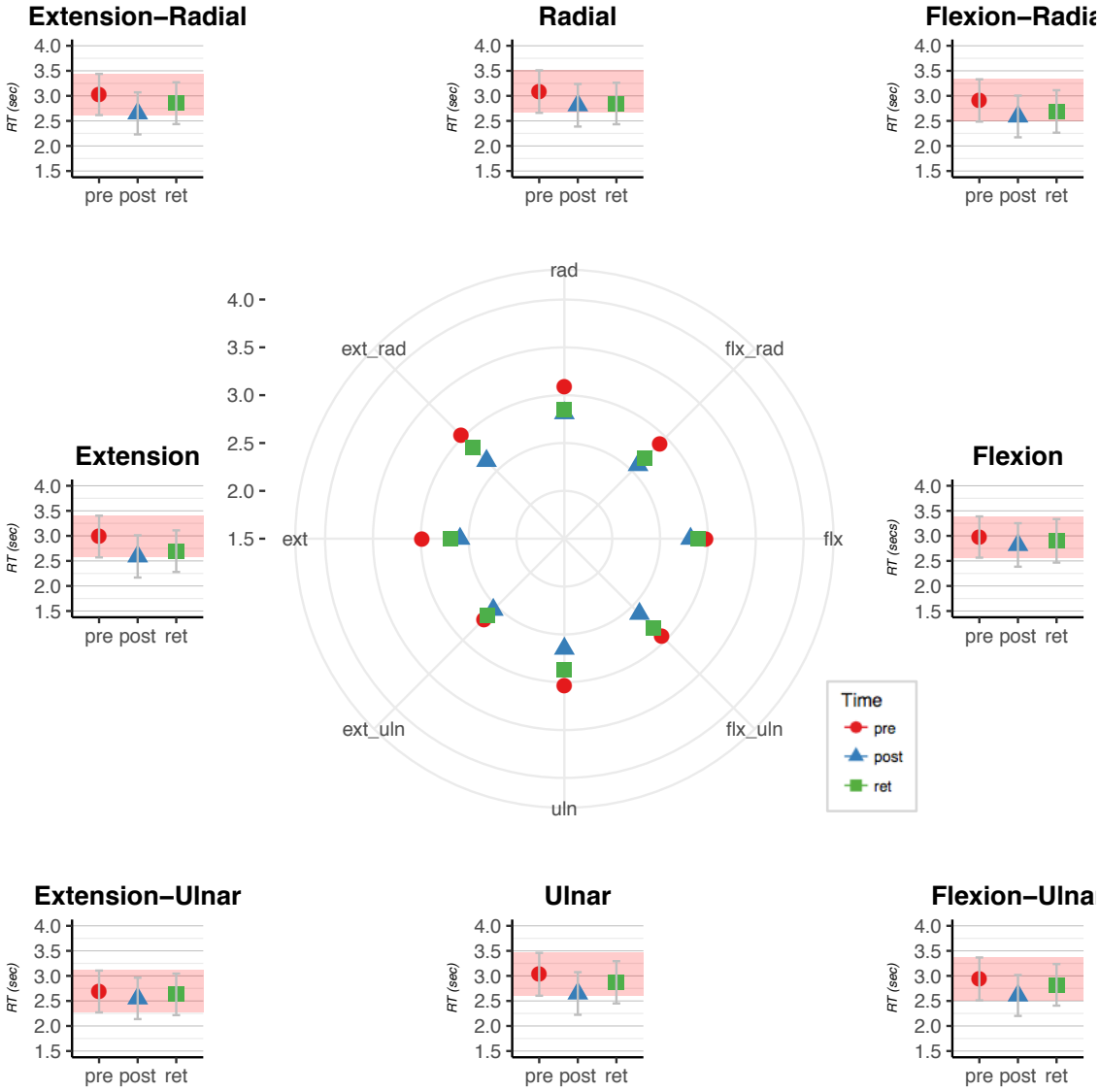

Figure 2.6-10 Changes in left-hand Peak Velocity for the training group across testing sessions. No systematic differences in Peak Velocity can be observed across sessions for any of the eight target locations.

Peak Velocity for the Control Group Left Hand

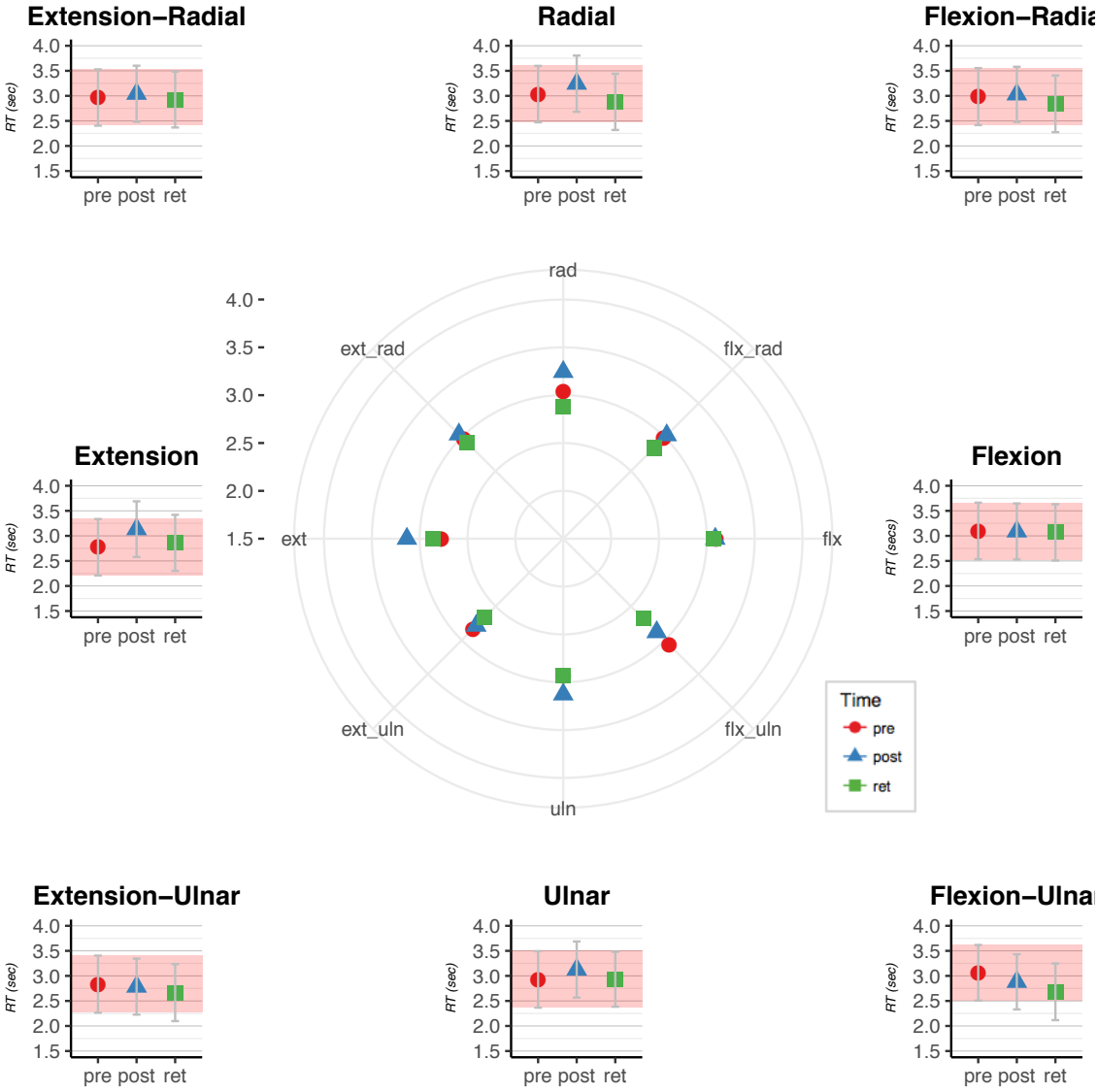

Figure 2.6-11 Changes in left-hand Peak Velocity for the control group across testing sessions. No systematic differences in Peak Velocity can be observed across sessions for any of the eight target locations.

Table 2.6-7 Pre-post and pre-retention contrasts in Peak Velocity for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	2.976	2.818	2.901	0.495	0.754	3.098	3.088	3.070	0.958	0.883
	flx_rad	2.908	2.588	2.689	0.163	0.363	2.985	3.029	2.841	0.821	0.454
	rad	3.085	2.812	2.847	0.236	0.303	3.035	3.243	2.880	0.268	0.410
	ext_rad	3.027	2.650	2.853	0.096	0.452	2.967	3.042	2.927	0.697	0.838
	ext	2.987	2.590	2.695	0.088	0.201	2.773	3.134	2.861	0.058	0.654
	ext_uln	2.689	2.550	2.631	0.543	0.809	2.835	2.786	2.666	0.797	0.380
	uln	3.032	2.649	2.872	0.095	0.507	2.931	3.127	2.933	0.294	0.992
	flx_uln	2.940	2.610	2.821	0.149	0.614	3.063	2.881	2.682	0.331	0.050

Table 2.6-7 Pre-post and pre-retention contrasts in Peak Velocity for the Training and Control Groups (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	3.259	2.692	2.841	**0.014***	0.075	2.954	2.686	2.989	0.174	0.847
	flx_rad	2.883	2.514	2.614	0.120	0.261	2.878	2.766	2.795	0.581	0.676
	rad	3.336	2.741	2.849	**0.011***	**0.040***	3.054	2.692	3.023	0.060	0.874
	ext_rad	3.015	2.504	2.842	**0.027***	0.464	3.044	2.654	2.671	0.057	0.058
	ext	2.945	2.424	2.575	**0.028***	0.126	2.804	2.600	2.697	0.316	0.596
	ext_uln	2.914	2.273	2.520	**0.006***	0.097	2.984	2.632	2.705	0.070	0.144
	uln	3.097	2.536	2.648	**0.020***	0.065	2.801	2.979	2.928	0.380	0.514
	flx_uln	3.104	2.667	2.855	0.061	0.289	2.907	2.771	2.871	0.486	0.853

2.6.11 Intervention Group Peak Velocity: Visuomotor Training Task

Mean Peak Velocity scores decreased across training day as the task got progressively more difficult. PV was lower on training Day 5 in comparison to Day 1 ($p<0.000$).

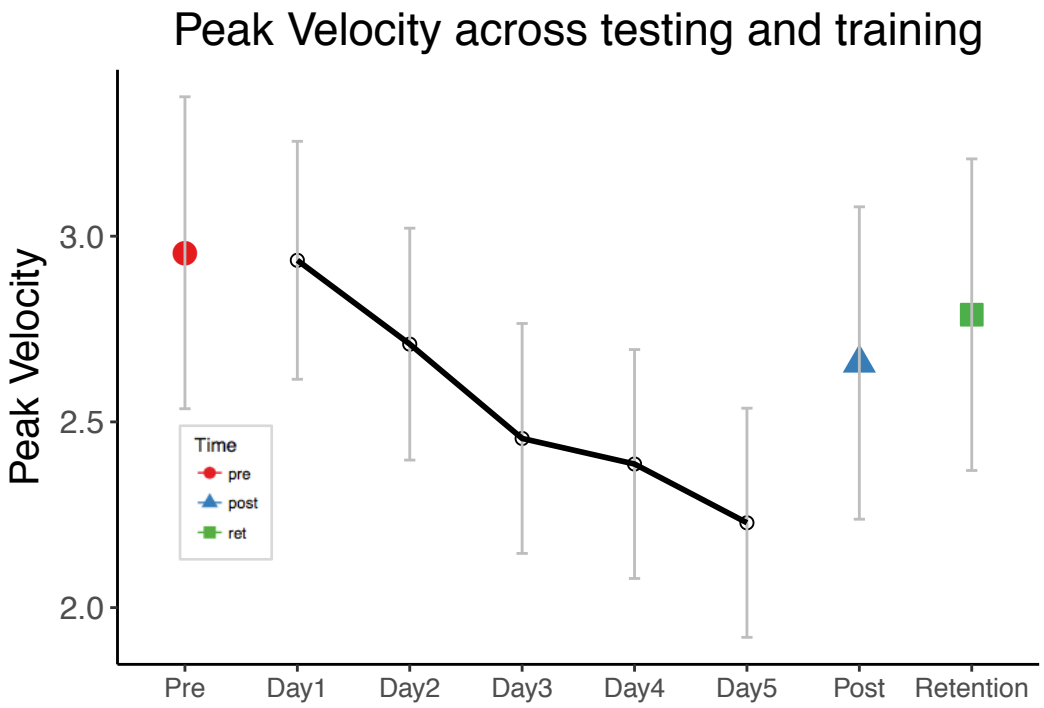

Figure 2.6-12 Changes in Intervention Group Peak Velocity across Testing Sessions and Training Days. The average PV across all targets is shown for each testing session: pre, post and retention. In addition, the average PV across training day is shown in the centre of the figure, connected with a black line. Mean PV on the visuomotor training task appears to decrease from training Day 1 to training Day 5. PV is slightly lower at the post-test following training than at pre-test, indicating a lower peak velocity in the movement trajectory. At the retention session, mean PV is also slightly lower than at pre-test.

Table 2.6-8 Mean Peak Velocity values by Training Day in the Visuomotor Training Task, and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	2.935 (0.163)	2.615, 3.255	-
Day2	2.709 (0.159)	2.397, 3.022	0.088
Day3	2.455 (0.158)	2.146, 2.765	**0.000***
Day4	2.387 (0.157)	2.078, 2.695	**0.000***
Day5	2.228 (0.157)	1.920, 2.537	**0.000***

* indicates $p<0.05$

2.6.12 Peak Velocity Time: Baseline Visuomotor Task

Peak Velocity time (PVT) is the time at which maximum velocity was reached during the interval between movement onset and target acquisition, or if participants failed to acquire the target, the interval between movement onset and timeout.

2.6.12.1 Motor Training Group

Left (training) limb: PVT was higher at the post-test session than at the pre-test session for the 'radial' (p=0.038) and 'extension-radial' (p=0.030) targets, indicating that peak velocity was reached at a later stage in the movement trajectory. PVT values for the remaining six target locations were not reliably different at post-test in comparison to PVT values at pre-test. At the retention test, no systematic differences were seen in PVT compared to the pre-test.

Right (transfer) limb: At the post-training session, PVT was systematically higher for the right limb for three out of the eight targets. These were the 'extension' (p=0.019), 'extension-ulnar' (p=0.028) and 'flexion-ulnar' (p=0.009) targets. The remaining five post-test target values were not reliably Changes in left-different from PV values at pre-test. At the retention test, PVTs remained higher than at the pre-test for the 'extension' (p=0.040) and 'extension-ulnar' (p=0.036) targets.

2.6.12.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for the left limb. For the right limb, PVT was lower at post-test for two targets: 'extension' (p=0.010) and 'extension-ulnar' (p=0.010), but these differences were not seen at retention. No reliable differences were observed between pre-test PVTs and retention session PVTs.

Peak Velocity Time for the Training Group Left Hand

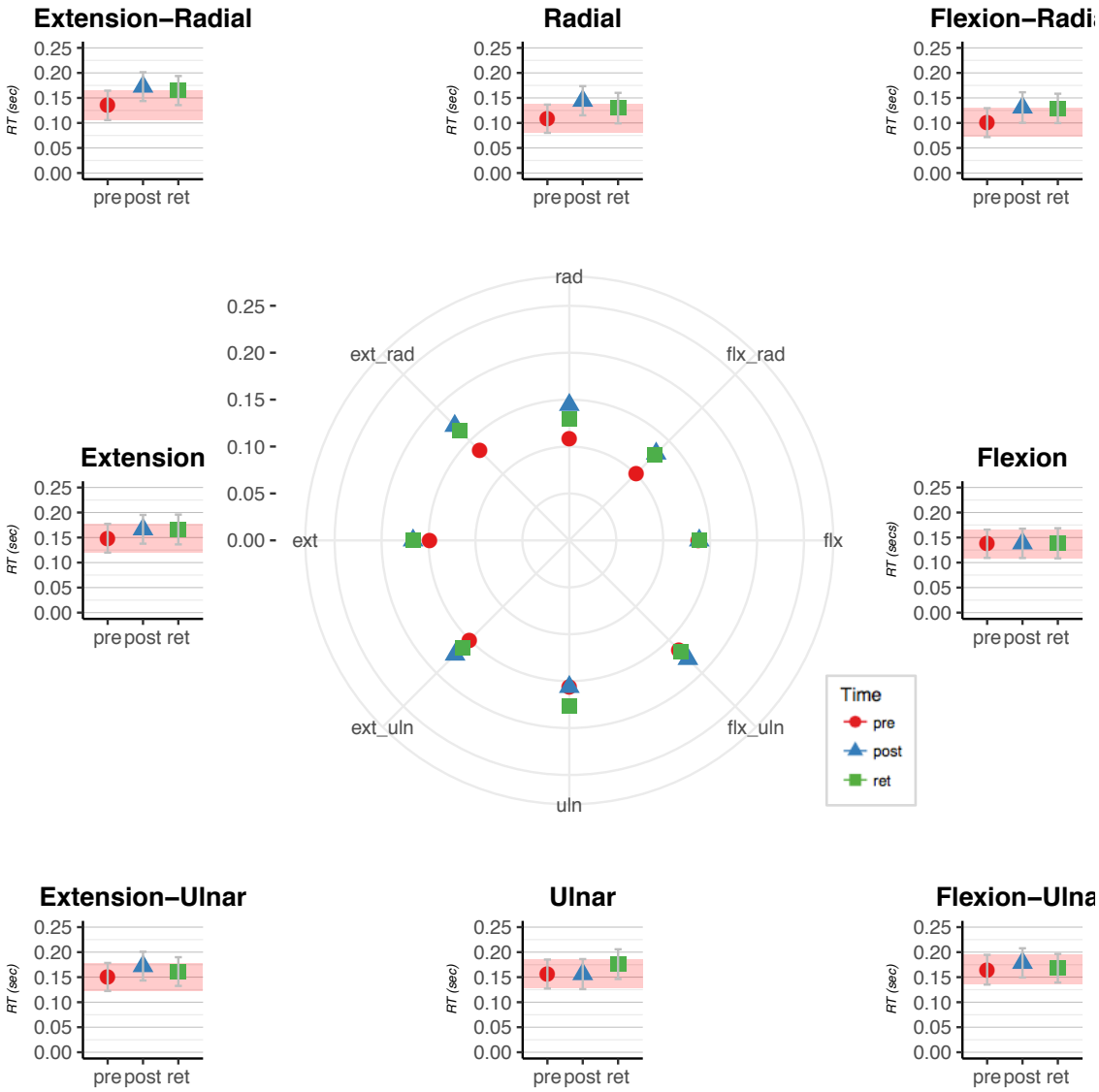

Figure 2.6-13 Changes in LH Peak Velocity Time for the Training Group across Sessions. Higher PVT scores were observed in the extension-radial and radial targets at post-test sessions, however this difference was not seen at retention. No other systematic changes in time at Peak Velocity were observed across sessions for the remaining targets.

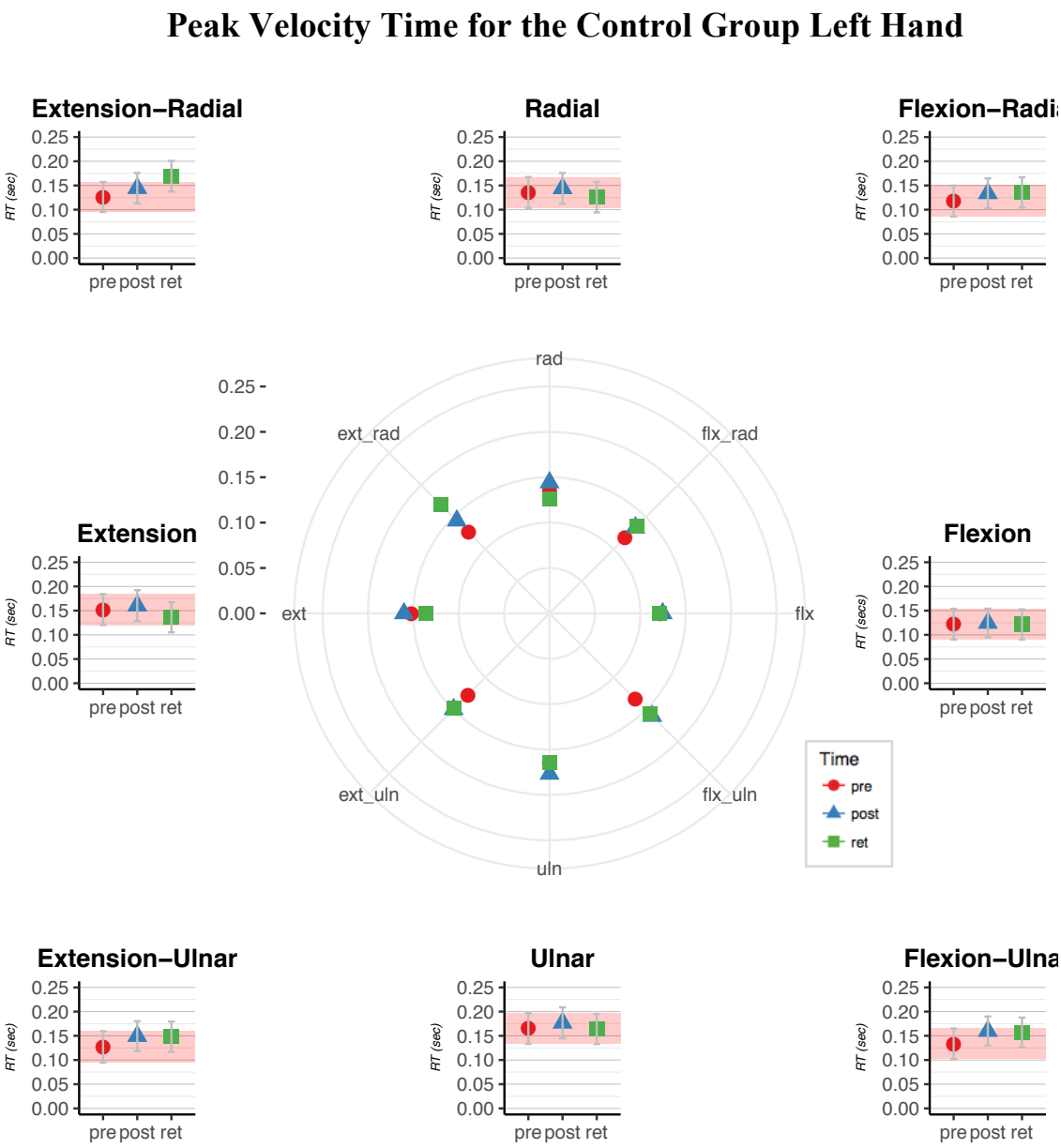

Figure 2.6-14 Changes in left-hand Time at Peak Velocity for the control group across testing sessions. No systematic differences in PVT can be observed at post-test sessions for any of the eight target locations. At retention, one difference is seen for the extension-radial target, with retention PVT higher than pre-test PVT.

Table 2.6-9 Pre–post and pre-retention contrasts of Time at Peak Velocity for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.138	0.138	0.139	0.962	0.956	0.122	0.125	0.121	0.891	0.975
	flx_rad	0.101	0.131	0.129	0.094	0.121	0.118	0.134	0.136	0.406	0.347
	rad	0.108	0.144	0.130	**0.038***	0.240	0.135	0.144	0.126	0.645	0.611
	ext_rad	0.135	0.173	0.165	**0.030***	0.090	0.126	0.144	0.169	0.331	**0.026***
	ext	0.149	0.166	0.166	0.297	0.309	0.152	0.160	0.136	0.673	0.401
	ext_uln	0.150	0.172	0.161	0.214	0.536	0.127	0.149	0.148	0.239	0.268
	uln	0.156	0.156	0.176	0.992	0.264	0.165	0.177	0.164	0.530	0.965
	flx_uln	0.165	0.179	0.168	0.453	0.863	0.134	0.160	0.157	0.157	0.216

Table 2.6-9 Pre–post and pre-retention contrasts of Time at Peak Velocity for the Training and Control Groups (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.131	0.154	0.133	0.183	0.931	0.141	0.166	0.143	0.189	0.922
	flx_rad	0.136	0.140	0.151	0.824	0.408	0.131	0.131	0.133	0.987	0.923
	rad	0.107	0.133	0.127	0.129	0.239	0.114	0.109	0.112	0.829	0.946
	ext_rad	0.143	0.155	0.172	0.530	0.106	0.156	0.141	0.140	0.441	0.399
	ext	0.147	0.188	0.183	**0.019***	**0.040***	0.142	0.192	0.163	**0.010***	0.292
	ext_uln	0.132	0.171	0.169	**0.028***	**0.036***	0.131	0.182	0.145	**0.010***	0.439
	uln	0.141	0.151	0.166	0.606	0.158	0.165	0.136	0.144	0.144	0.279
	flx_uln	0.147	0.193	0.159	**0.009***	0.518	0.151	0.172	0.158	0.279	0.733

2.6.13 Intervention Group Peak Velocity Time: Visuomotor Training

Peak Velocity Time was higher at Day 5 in comparison to Day 1 (p=0.029), indicating that as task difficulty increased, time at peak velocity came later during the movement trajectory.

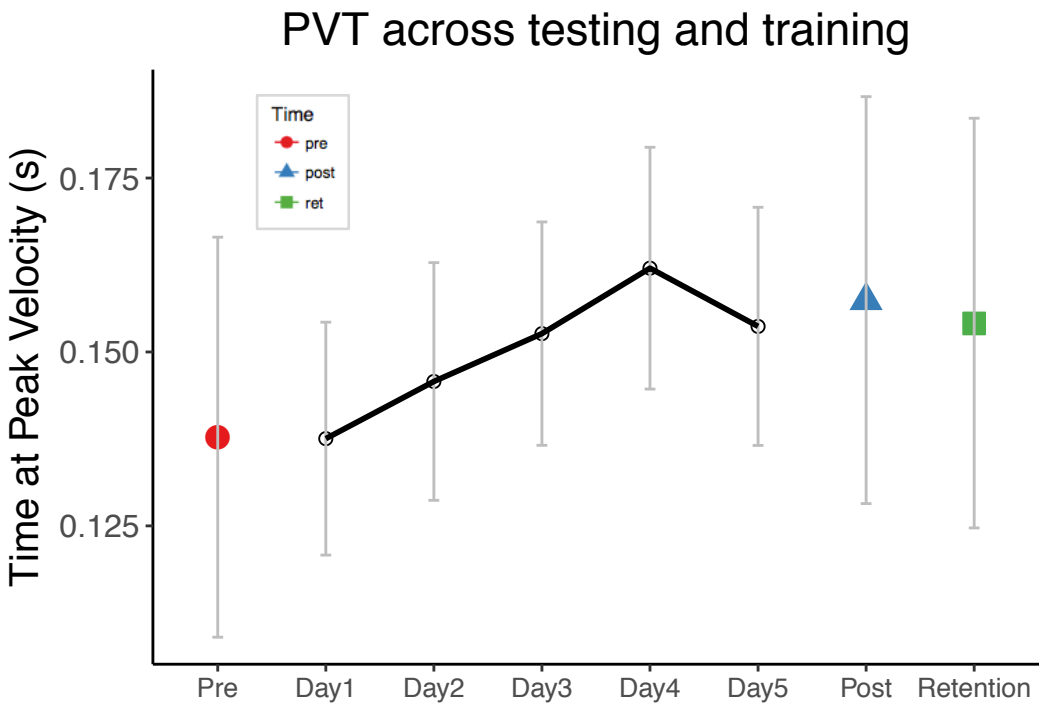

Figure 2.6-15 Changes in Intervention Group Time at Peak Velocity across Testing Sessions and Training Days. The average PVT across all targets is shown for each testing session: pre, post and retention. In addition, the average PVT across training day is shown in the centre of the figure, connected with a black line. Mean PVT on the visuomotor training task appears to increase from training Day 1 to training Day 5. Mean PVT is slightly higher at the post-test following training than at pre-test, indicating a later peak velocity in the movement trajectory. At the retention session, mean PVT is also later than at pre-test.

Table 2.6-10 Mean Peak Velocity Time values by Training Day in the Visuomotor Training Task, and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	0.138 (.009)	0.121, 0.154	-
Day2	0.146 (.009)	0.129, 0.163	0.278
Day3	0.153 (.008)	0.137, 0.169	**0.048***
Day4	0.162 (.009)	0.145, 0.179	**0.002***
Day5	0.154 (.009)	0.137, 0.171	**0.029***

* indicates p<0.05

2.6.14 Heading Error at 100ms

Heading Error at 100ms (HE) is the difference between desired heading and actual heading, calculated in a 10ms window centred 100ms following movement onset. Heading deviation was taken as a measure of the efficiency of *feedforward* processes, as it was assumed that adjustments of movement trajectory facilitated by visual feedback of the cursor were not possible prior to 100ms. Values closer to zero indicate lower heading error.

2.6.14.1 Motor Training Group

Left (training) limb: For all but one target, HE values were not reliably different at post-test in comparison to PVT values at pre-test. HE for the 'flexion-radial' ($p=0.001$) target only was lower (more negative) at the post-test session than at the pre-test session, indicating a larger heading error at post-test. At the retention test, no systematic differences were seen in HE compared to the pre-test.

Right (transfer) limb: At the post-training session, PVT was systematically higher for the right limb for two out of the eight targets. These were the 'extension-ulnar' ($p=0.038$) 'flexion-radial' ($p=0.007$), 'radial' ($p=0.002$) targets. The remaining five post-test target values were not reliably Changes in left-different from PV values at pre-test. At the retention test, no systematic differences in HE were observed in comparison to the pre-test.

2.6.14.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for the left limb. For the right limb, PVT was lower at post-test for two targets: 'extension-radial' ($p=0.004$) and 'flexion-ulnar' ($p=0.038$); and for the 'extension-radial' target, this difference was also seen at retention ($p=0.006$). No other reliable differences were observed between pre-test HE and retention session HE amongst controls across session.

Heading Error at 100ms for the Training Group Left Hand

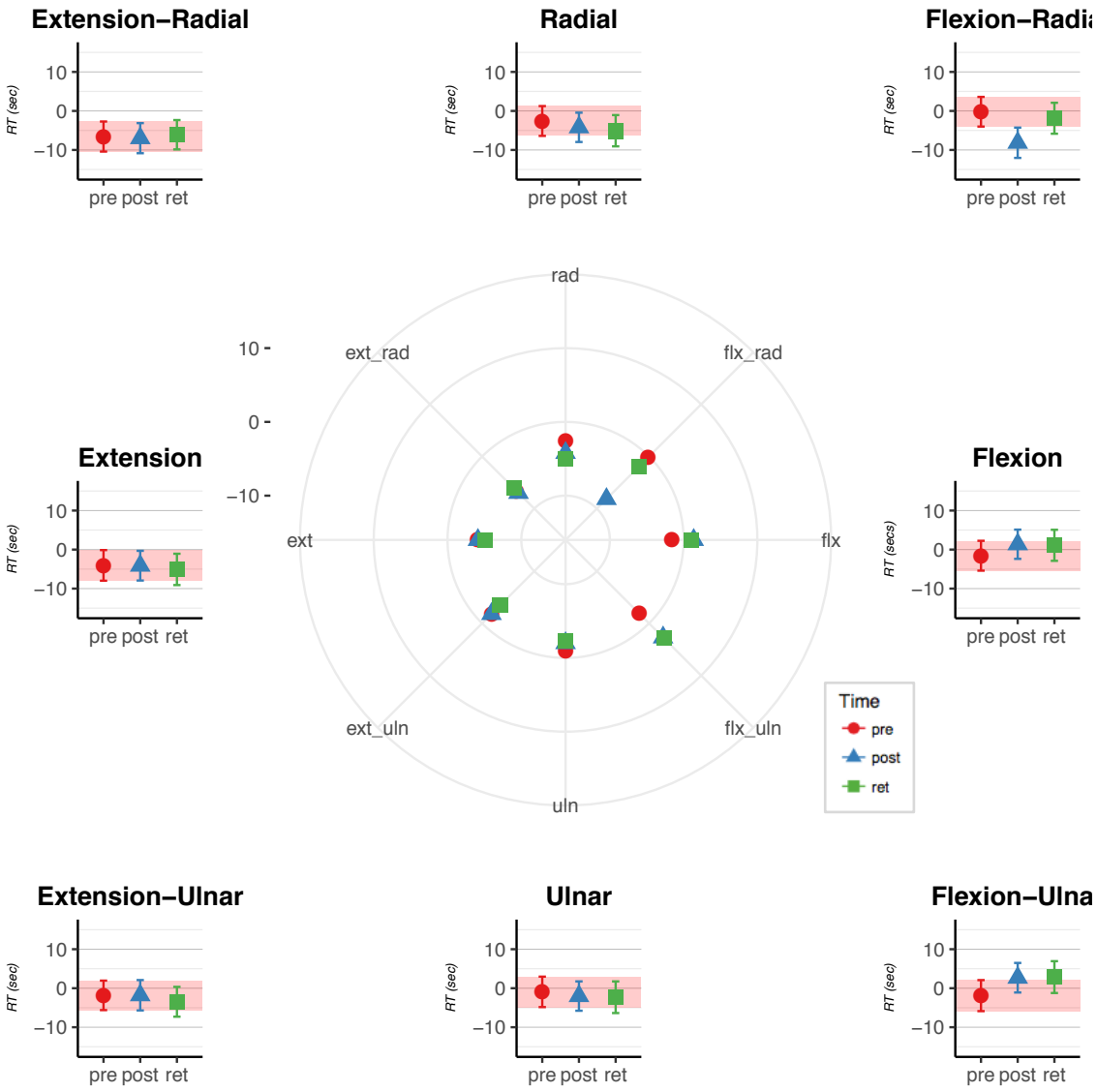

Figure 2.6-16 Heading error at 100ms for the training group left hand across testing sessions. HE is lower (more negative) at the flexion-radial target at post-test. HE values closer to zero indicate less error. No other reliable differences in HE can be seen across sessions for the remaining targets.

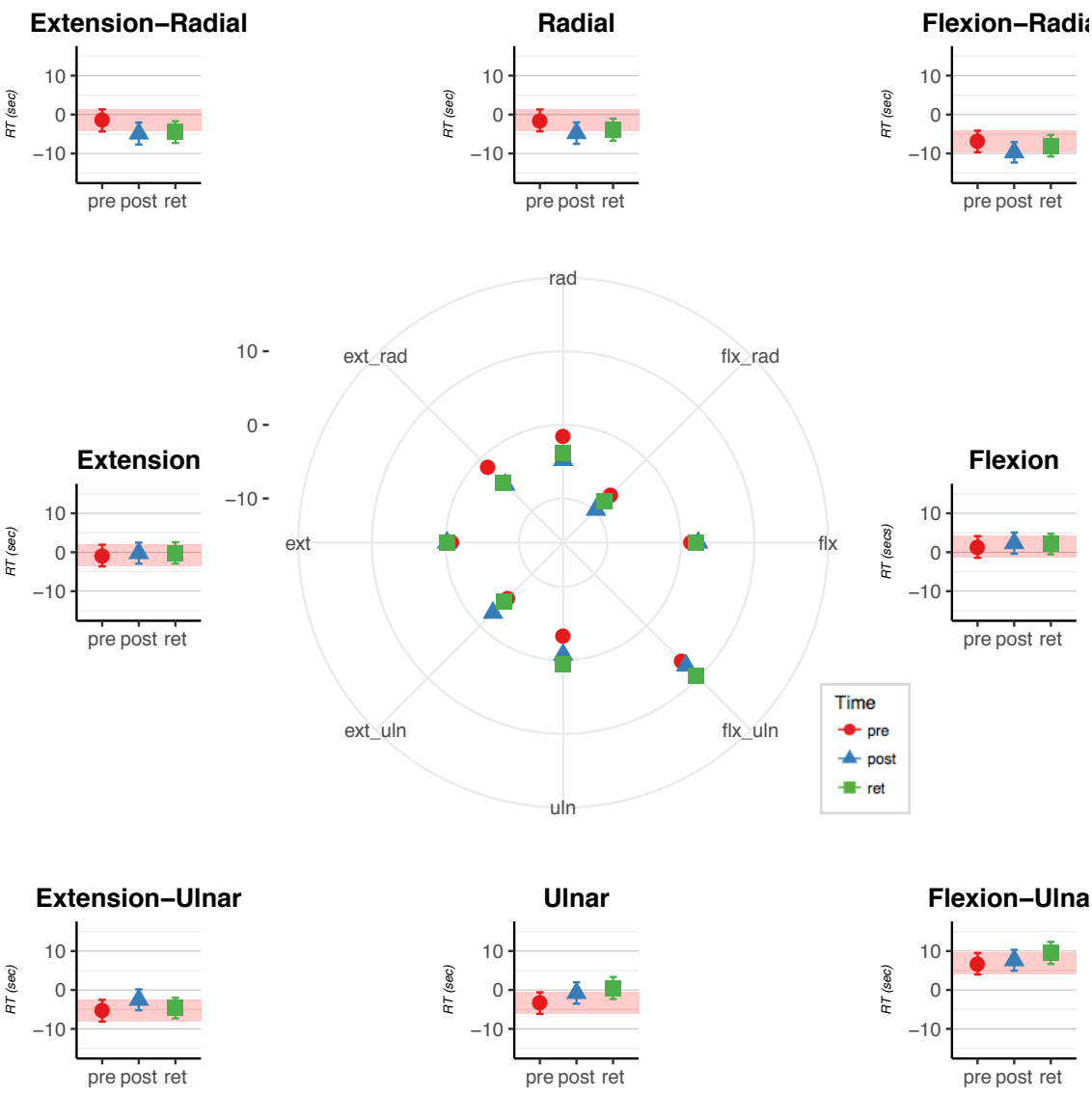

Figure 2.6-17 Heading error at 100ms for the control group left hand across testing sessions. No reliable differences in HE can be seen across sessions for any of the eight targets.

Table 2.6-11 Pre-post and pre-retention contrasts in Heading Error for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	-1.577	1.365	1.096	0.233	0.287	-1.476	0.658	2.591	0.382	0.096
	flx_rad	-0.202	-8.157	-1.874	**0.001***	0.495	-7.884	-9.381	-5.642	0.559	0.365
	rad	-2.575	-4.204	-5.070	0.505	0.306	-2.091	-6.230	-4.954	0.102	0.255
	ext_rad	-6.563	-6.978	-6.101	0.866	0.843	-5.702	-10.519	-4.820	0.053	0.733
	ext	-4.054	-4.124	-5.083	0.977	0.677	-4.710	-6.217	-5.550	0.554	0.743
	ext_uln	-1.831	-1.800	-3.475	0.990	0.498	-5.718	-6.917	-10.659	0.645	0.057
	uln	-0.934	-2.011	-2.308	0.652	0.582	0.312	-3.516	0.598	0.131	0.911
	flx_uln	-1.893	2.690	2.853	0.058	0.057	10.575	10.022	9.292	0.831	0.615

Table 2.6-11 Pre-post and pre-retention contrasts in Heading Error for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	-0.393	0.739	0.850	0.652	0.622	-0.452	0.761	1.205	0.626	0.512
	flx_rad	4.195	10.800	7.435	**0.007***	0.196	4.171	7.770	9.138	0.169	0.060
	rad	4.198	11.825	8.019	**0.002***	0.128	3.758	7.744	5.835	0.118	0.403
	ext_rad	3.997	6.278	2.462	0.348	0.530	0.864	8.288	7.682	**0.004***	**0.006***
	ext	0.072	2.098	0.544	0.418	0.847	-0.435	1.607	2.102	0.445	0.322
	ext_uln	5.664	5.331	3.720	0.895	0.447	2.884	2.599	3.168	0.909	0.910
	uln	2.145	1.356	2.427	0.739	0.909	3.662	1.444	1.907	0.383	0.497
	flx_uln	-2.167	-4.627	-5.134	0.323	0.216	-6.330	-1.352	-5.588	**0.038**	0.765

2.6.15 Intervention Group Heading Error at 100ms: Visuomotor Training

No difference was observed in Heading Error at 100ms between Day 1 and Day 5 (p=0.884), and no reliable changes can be seen across training days, despite increasing task difficulty.

Table 2.6.12 Mean Heading Error at 100ms for each Training Day in the Visuomotor Training Task, and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	-1.169 (0.479)	-2.109, -0.229	-
Day2	-0.689 (0.479)	-1.628, 0.251	0.451
Day3	-0.668 (0.485)	-1.619, 0.282	0.431
Day4	-0.691 (0.470)	-1.611, 0.230	0.440
Day5	-1.081 (0.475)	-2.013, -0.150	0.884

* indicates p<0.05

2.6.16 Overall Adaptation to the Visuomotor Task

In order to derive an overall measure of the adaptation that occurred over the course of the training period, we first sought to determine separately for each target, the manner in which systematic variations (i.e. adaptations) in the five variables that characterised the movement trajectory (SAL, PD, PV, PVt, HE) accounted for changes in the primary measure of performance i.e. movement time. To this end, elastic-net penalised general linear regression was used to obtain an optimal set of weighted coefficients for the five predictor variables (i.e. SAL, PD, PV, PVt, HE). The residual representing the difference between the observed MT and the MT predicted by the model was obtained for each participant, and scaled by the intercept derived for the model (effectively the mean MT for each respective target). These scaled residuals were averaged across the eight targets to produce a single composite measure of adaptation for each participant.

2.6.17 Relationship between Visuomotor Task and Cognitive Results

To establish whether there were relationships between the measures of adaptation derived for the individual participants to the baseline motor task, and the degree of improvement exhibited by those individuals on the tests of cognitive function, statistical measures of association (Percentage Bend correlations (Wilcox, 2012) and robust linear regressions) were calculated. With a view to reducing the experiment-wise inflation of alpha that would otherwise arise as a result of conducting multiple inferential tests, these were generated only for assessments of cognitive function for which reliable changes from pre- to post-intervention had been obtained. No reliable associations between the composite measure of adaptation and changes in cognitive test scores were observed.

2.7 Discussion

In this study, we assessed whether a period of motor training, undertaken by older adults in the context of a challenging coordination task, extending over the course of five days, would lead to improved performance on tests of cognitive function. It was hypothesised that individuals who participated in a coordinated visuomotor training intervention would derive greater benefits in terms of cognitive function than an active control group, who were engaged in an otherwise equivalent task with no requirement for coordinated movement. It was observed that coordination training led, in particular, to enhanced performance on the Choice Reaction Time Task, the SART, and elements of the Dual n-Back task.

With respect to the CRT, individuals in the coordination training group exhibited latencies for both the "cognitive" and "motor" elements that were shorter during post-intervention assessment than those recorded prior to the intervention. In contrast, individuals in the active control group did not exhibit such changes. As the motor training task emphasised speed of execution, with the participants encouraged to hit targets appearing onscreen as quickly and accurately as possible, it is likely that the decrease in "motor reaction time" i.e. movement time, is a manifestation of 'near' transfer between tasks that share common (motor) elements. Although the rapidity with which the movements were initiated was not emphasised as a goal of the training task, it is conceivable that the participants may have interpreted the instructions in this fashion. A subsidiary analysis of reaction times associated with the training movements undertaken during the intervention (Appendix 1) revealed that these did not change reliably over the five-day period. It was however the case that the RTs associated with the visuomotor assessment task decreased consistently from pre- to post-intervention, for six of the eight target locations (Appendix 2). It is therefore also possible to interpret the decrease in the "cognitive" element of the CRT – which corresponds closely to the RT measure derived for the visuomotor assessment task, as a further manifestation 'near' transfer between tasks that share common elements. Moreover, this highlights the importance in appropriately (and conservatively) interpreting some of the measures used customarily to assess "cognitive function", both in the context of interventions that encompass physical responses, and in those that do not. Indeed, many "physical activity" interventions have similar 'movement' task characteristics to those which characterise several cognitive assessment tools. The implications of this are that the interpretations

that can be drawn from cognitive outcome measures are limited; we cannot reliably state that 'wide' transfer to a task very different from the training task has occurred.

It is also notable that when assessed eight to ten days following the cessation of the intervention, the effects obtained for the CRT measures were diminished. This provides additional support that observed results were not merely practice effects, as performance at retention, where participants carried out the test for a third time, did not show reliable improvements. It also suggests that at least some of the benefits seen in transfer to the cognitive domain are restricted to immediately following the intervention. It may be that the duration of effects seen after training is correlated with the duration of the training period (dose), so that longer interventions are required to see lasting cognitive benefits. It is notable that there is often a lack of retention or 'follow-up' measures in interventions in this domain (e.g. Lauenroth, Ioannidis & Teichmann, 2016). This finding highlights the importance of including a retention session in experimental design, so that the duration of any observed effects can be further explored.

In relation to the visuospatial n-Back task, no changes were seen in the easiest '1-back' task condition, in terms of either accuracy or RT measures for either group. This may constitute evidence of a "ceiling effect". However, in the 2-back condition, the control group improved systematically on measures of visual accuracy. In the Dual n-back task, the motor training group improved performance on the reaction time measures, both visual and auditory, whereas the control group showed no improvement on these measures. Interestingly, the control group improved on measures of auditory accuracy in the 2-back condition at the post-test session. These findings support the notion that the training group primarily exhibited improvements in the RT measures. Conversely, the active control group tended to show improvements in the accuracy measures derived for this task. As the control task involved memory and attention in order to remember and update the number of targets appearing with specific characteristics, it is possible to interpret this pattern of outcomes as evidence that there was some degree of positive transfer from the 'active control' task to these specific measures of executive function. Again, we see that RT measures have improved for the training group. In addition, only the control group exhibited faster RTs on the baseline motor task following intervention (Appendix 2). These changes in performance could be viewed in a similar light to the RT measures for the CRT; perhaps the interpretations that can be drawn here in relation to 'transfer' to the cognitive domain is limited; again we cannot reliably state that 'wide' transfer from the motor training task to a cognitive task has occurred.

Both groups improved performance on the Sustained Attention to Response Task, with the Motor training group making fewer Omission errors post-training and during the retention session, and both training and control groups exhibiting fewer Commission errors both post-test and during the retention session. It has previously been suggested that the SART is not susceptible to practice effects (Robertson et al., 1997; Di Rosa, 2014). In this regard, attention should be drawn to the similarities between the activities undertaken by both groups of participants during the intervention period and the nature of the SART. The individuals in both groups (motor training and active control) were required to concentrate intensely over four 4-minute blocks. This requirement is similar to the four-minute SART task. The SART task is a task measuring sustained attention in which participants are required, over a 4-minute period, to continuously respond to visual stimuli (the numbers 1-9) by clicking a mouse every time a number appears on the screen, with the exception of the number 3. It is thought that lapses of attention cause participants to commit errors on this task (Robertson et al, 1997). Thus, although practice effects cannot be ruled out, it seems reasonable to conclude that both of the tasks performed during the intervention period engaged sustained attention, which led to improvement on the SART. It is also pertinent to note that in all cases, the magnitude of the improvements in SART performance were greater for the motor training group, who displayed larger mean reductions in the number of errors, and greater effect sizes derived for these differences.

The motor training gave rise to changes in performance on the baseline motor task, with the training group exhibiting shorter movement times and lower path deviation at the post-test session. It has been shown that practice on a motor task leads to modification of the patterns of muscle synergies used, and gives rise to improved efficiency of motor commands that optimise the recruitment of such synergies (Carson & Riek, 2001). The demonstration of interlimb transfer is another level of support for the hypothesis that training on a complex coordination task can lead to neuronal adaptations, and it is our hypothesis that such changes are the basis upon which transfer to performance on the cognitive task was based.

Interlimb transfer, expressed as change in the performance of the untrained limb, was measured to assess the generality of the adaptations that arose from the five days of training. It has been suggested that neural adaptations mediate performance gains following unilateral training on motor tasks (e.g. Hinder et al. 2011; Hellebrandt, 1951; Ruddy et al., 2016). Motor training consisting of short-term unilateral training of finger or thumb movements has been shown to engender bilateral increases in movement

characteristics, such as movement velocity, and in addition, greater increases in excitability of corticospinal projections to the muscles of the untrained limb (e.g. Carroll et al. 2008; Lee et al. 2010; Hinder et al. 2011). Using constrained spherical deconvolution, Ruddy et al., (2016) recently characterised the white matter pathways connecting specific cortical regions to their inter-hemispheric counterparts, and found that connections between specific nodes of the cortical motor network play a central role in transfer of performance on a motor training task. Moreover, it was revealed that structural characteristics of the interposed white matter pathways were associated with the level of transfer observed. Thus, measures of interlimb transfer provide us with a means of examining the generality and robustness of learning, and we can infer from transfer that neural adaptations have occurred in response to the training demands.

The increase in the straightness of the trajectory exhibited by the training limb did not give rise to inter-limb transfer, with the post-intervention untrained (right) limb scores similar to pre-test scores. However, interlimb transfer was apparent following the motor training task for measures of Path Deviation at the retention session. PD was lower for four targets in the trained limb at the post-test and retention session, and was lower for three targets in untrained limb performance at the retention session. These differences were not observed in control participants. Interlimb transfer was also noted in measures of Peak Velocity, which was reliably lower following training in the untrained limb for six targets. This effect was not accompanied by changes in PV for the trained limb following training. In addition, SAL was higher in the untrained limb in three target locations following training, but again changes in SAL were not seen in the trained (left) limb at the post- or retention-tests. Despite the absence, in the case of SAL and PV, of reliable changes in performance of the trained limb, it is nonetheless apparent that changes in the right limb performance were observed among motor training participants only. There existed the opportunity for individual participants to vary the degree to which they achieved a balance between changes in peak velocity and straightness of the trajectory – expressed ultimately in terms of movement time. In addition, the nature of this balance (or trade-off) may not have been equivalent across target positions, or even across limbs– due to the influence of neuromusculoskeletal constraints. Thus we can infer that neural adaptations associated with interlimb transfer of skill occurred following training.

In line with studies suggesting that in physical activity interventions, changes in cognitive outcomes are not mediated by changes in levels of aerobic fitness (Etnier et al., 2006), and evidence that greater cognitive benefits are observed following physical

activity interventions that include an element of motor fitness training (e.g. Oswald, 2006; Moreau et al., 2015), our research supports the hypothesis that factors additional to increased cardiovascular fitness in physical training interventions can contribute to the improved performance seen on cognitive outcome measures (Diamond & Ling, 2016; Morea et al., 2015). In addition, in the current study, we have shown that motor training leads to specific improvements on choice reaction time and working memory reaction time measures, suggesting that complex 'whole-body' movement training is not compulsory in producing such improvements. Only one isolated joint (with motion in two degrees of freedom) was involved in the coordination task used in the present study, yet several muscles act to generate motion in two degrees of freedom at this joint (principally Flexor Carpi Radialis, Extensor Carpi Radialis, Flexion Carpi Ulnaris, and Extensor Carpi Ulnaris) and sophisticated neuromuscular control is required to accomplish the very precise movements (the target zone was 1 degree of joint displacement) that were necessary to acquire the targets. Engagement of movement planning and visuospatial integration meant that many aspects of the task were similar to those measuring the cognitive outcomes following whole body coordination programmes (e.g. Forte et al., 2013; Voelcker-Rehage et al., 2010). In addition, given the relatively intense nature of the training intervention that required everyday practice for a week (in contrast to the majority of physical activity interventions that require weekly practice spread over 3-12 months), this finding demonstrates that efficacious changes in performance can be observed over a much shorter time period.

A perennial problem in randomised controlled interventions attempting to enhance executive functions is that control groups do not match training groups in important task characteristics (aside from the variable of interest). In order to adequately infer that cognitive outcomes were not due to placebo effects or other confounding psychological phenomena (e.g. motivation), it should be ensured that the active control group participants have equivalent expectations of improvement to the training group (Boot, Simons, Stothart & Stutts, 2013). This was accomplished here firstly by ensuring participants were not aware they were in a 'control' group, and by providing the same amount of social contact with both groups, as potentially social engagement could lead to cognitive effects (e.g. Scarmeas et al., 2001). The assessor carrying out the pre, post and retention test cognitive motor measures was blinded to the group allocation of all participants, to prevent experimenter expectations from influencing the results. And in addition, we trained controls on an adaptive task in which they were required to count and remember the number of target stimuli that diminished progressively over the course

of training. However, as a consequence, it appears that the active intervention had an impact on certain outcome measures, such as the SART and components of the Dual n-Back task. The control task in this experiment required the retention and updating of a particular variable, which bears similarities to a working memory task. As noted above, this is potentially the reason for control group improvements on accuracy measures in the Dual 2-Back task. Attentional demands were also identical for both groups, and this is reflected in similar improvements in the SART. This finding highlights the importance of the inclusion of active control tasks, as a basis upon which to support claims concerning the mechanisms that may have mediated the effects of the target intervention. If this control task did not hold equivalent attentional demands and require similar levels of task engagement due to its adaptive nature, the underlying reason for changes in the cognitive outcome measure may have been misinterpreted, and attributed wholly to the motor component of training. This further emphasises the inadequacy of controls used in other investigations that do not have similarly 'adaptive' or engaging control tasks (Boot, Simons, Stothart & Stutts, 2013; Rosnow & Rosenthal, 1997). Indeed, it might be advisable to include the SART or another sustained attention task as a matter of course, as a means of verifying that the attentional demands of both the training and active control interventions were equivalent.

A subsidiary objective was to determine the nature of the adaptations to the coordination-training regime, which may have mediated the positive transfer to the cognitive domain. It was first necessary to derive an empirical measure of adaptation that was sensitive to (potentially) independent variations in the parameters that characterised the movement trajectory, and to differences in the degree of their covariation across target locations. This was achieved using the technique of elastic net regularisation to obtain weighting coefficients for each parameter, and for each target. These were in turn used to generate a composite measure of adaptation for each participant. No reliable associations between this measure of adaptation to the training task and the cognitive outcome measures were observed. It is of course possible that homogeneity in the strategies that participants used to adapt to the motor training task was sufficient as to preclude adequate differentiation of individual performance, and thus to demarcate correlational relationships of this nature.

Conclusion

Overall these results provide partial support for the hypothesis that training on a motor coordination task can lead to improved performance on tests of cognitive function,

with some marked differences exhibited between the training and active control groups. It demonstrates that motor training tasks involving movement planning, multisensory integration and the precise coordination of muscle recruitment, such as rapid-aiming arm movement tasks, can lead to improved performance on measures of cognitive function. Moreover, these changes were not observed in an active control group. However, it is necessary to further unravel whether such effects are indeed attributable to changes in 'cognitive' function and constitute 'wide' transfer to the untrained cognitive domain. In addition, a more difficult task is needed in order to derive sufficiently heterogeneous measures of adaptation to the motor task, in order that any associations with cognitive outcome measures can be explored.

Chapter 3 Can deferral of visual feedback in a coordination training task engender enhanced cognitive transfer?

3.1 Introduction

Recent physical training interventions that emphasise motor fitness have been shown to lead to improvements in executive function (e.g. Berryman et al. 2014; Forte et al, 2013; Johan et al., 2016; Moreau et al., 2015; Niemann et al., 2014; Pesce et al., 2013; Schoene et al., 2015; Voelcker-Rehage et al., 2011). However, many current studies looking at coordination training tend to do so at a 'superficial' level. Researchers take an activity that is conceptualised as involving accentuated motor control, such as dance (e.g. Niemann et al., 2016) or yoga (e.g. Gothe et al., 2013), and then infer that benefits in cognitive performance are related to the motor activity. However, without directly measuring the adaptations to the motor intervention, these types of inferences are hard to validate. The relationship between motor-training interventions and cognitive function needs to be understood at a more elementary level; and insights from the field of motor learning can be applied to aid in such an endeavour.

Centre-out target acquisition tasks are one such task that has been studied extensively in the motor control literature. Building on the paradigm introduced in Experiment 1, in which training on a coordinated wrist movement task led to improvements on performance on a number of executive function tasks, we can use this methodology to explore the task demands that are related to transfer to the cognitive domain. In experiment 1, we utilised a method for controlling the exact dose of training that individuals receive, and allowed measurement of the key movement characteristics involved in adapting to the motor task. In extending this line of investigation, it is important to determine the dimensions of motor task complexity that are instrumental in bringing about positive transfer to cognitive function – at least as this is expressed via tests of executive function.

It has previously been shown that the type of visual feedback provided during a visuomotor task influences the nature of the adaptation to the task (e.g. Hinder et al., 2008; Schween & Hegele, 2017). Presently influential models of motor learning frequently conceptualise learning as arising predominantly from updating internal models using 'sensory-prediction errors', for example the disparity between predicted

and actual cursor position (Tseng et al. 2007; Wolpert et al. 1998). However recent studies (e.g. Hinder et al., 2008; Bond & Taylor, 2015) have shown that alternative strategies can be engaged in the context of visuomotor adaptation. Hinder, Tresilian, Riek & Carson (2008) investigated the role played by the type of visual feedback that was provided during a period of adaptation to a visuomotor rotation, on the nature of the performance that was expressed subsequently following removal of the rotation. Of particular significance in the present context is the contrast between a (standard) condition in which the participants received either continuous feedback of the cursor during each attempt to acquire a target, and those in which visual feedback was provided only following completion of the aimed movement. The latter mode of feedback took the form either of a display of the complete movement trajectory, or only the terminal position. Prototypical aftereffects were observed when participants had received online (i.e. 'concurrent') feedback of their cursor trajectory during the adaptation phase. In marked contrast, aftereffects were either absent or markedly diminished in the two conditions in which deferred visual feedback was provided. The authors surmised that participants who received only post-trial feedback necessarily relied to a greater degree on (pre-initiation) movement planning in order to improve their performance on the adaptation task. It was also supposed that to the degree that these conditions promoted explicit (as opposed to unconscious or "automatic") learning, rapid redeployment of the set of motor commands appropriate to the un-rotated environment would also be supported.

More recently, Bond and Taylor (2015) reported that in tasks whereby post-trial feedback was provided, such 'explicit' forms of learning were remarkably flexible or 'changeable' in comparison to more rigid 'implicit' forms of learning seen in tasks that provided concurrent visual feedback of cursor position. In other words, explicit learning strategies could rapidly accommodate novel task demands, such as new target locations or changes in visual perturbations, but with increasing task complexity, there was a corresponding decrease in 'implicit' learning.

'Explicit' learning strategies have been proposed to constitute the early or 'fast' process involved in learning (e.g. McDougle, Bond & Taylor, 2015) which has been associated with cerebellar and parietal brain regions (Flament et al., 1996; Seidler & Noll, 2008). Recently, it has been shown amongst patients with cerebellar dysfunction that not only were deficits observed in 'sensory-prediction-based-learning' processes traditionally ascribed to the cerebellum, but also deficits in developing or maintaining aiming strategies in response to visual perturbations (Butcher et al., 2017). This, the

authors suggest, implicates the cerebellum in a network involved in learning action-outcome associations. Thus, we believe a task variant in which visual feedback is deferred, networks traditionally describe as both 'motor' and 'cognitive' will be engaged to improve task performance.

The premise that motivates the current study is by manipulating the provision of feedback in the appropriate manner (i.e. giving post-trial feedback), it will be possible to increase the level of explicit learning that occurs in a visuomotor training task. The related conjecture is that explicit forms of motor learning – in necessarily drawing upon neural resources that mediate cognitive function, are likely to promote greater positive transfer to the cognitive domain, than implicit/unconscious forms of motor learning.

***Hypothesis*:** A complex motor training intervention designed to accentuate multisensory integration, movement planning, the precise coordination of muscle activity and 'explicit' learning strategies will improve performance on measures of executive function in older adults to a greater degree than an active control intervention.

3.2 Materials and Methods

3.2.1 Participants

67 healthy community-dwelling older adults were recruited using ageing research databases, local community groups and online volunteer boards. 7 participants dropped out before completion (two due to illness, one due to equipment failure, three due to unforeseen schedule clashes), leaving 60 participants in total (65-88 years, Mean= 70.07, SD= 5.5, Males= 27, 45%).

Participants underwent telephone screening prior to enrolment in the study, to exclude anyone with evidence of neurodegenerative disease. Participants were pre-screened using a telephone adaptation of the MMSE (Newkirk et al., 2004) and a health screening questionnaire to exclude anyone with evidence of neurodegenerative disease. All participants were right-handed as assessed using the Edinburgh Handedness Inventory (Oldfield, 1971; mean Laterality Quotient: +89.4). Participants were aged over 65 (65-88 years, Mean=70.1, SD=5.5, 27 Males). All participation was voluntary, and all participants provided written informed consent to the procedures, which were approved by the Trinity College Dublin School of Psychology Ethics Committee and conducted in accordance with the Declaration of Helsinki.

3.2.2 Intervention

A blinded randomised controlled trial was carried out over the course of four weeks. Participants were randomly assigned to one of two conditions: motor training (n=30) or active control (n=30). Groups did not differ significantly in terms of age ($t(33)=0.45$, $p=0.673$) or gender (X-squared = 1.5273, df = 1, p-value = 0.2165). Both groups attended initial 'pre-test' sessions, where a host of cognitive and motor assessments were carried out (outlined below). Subsequently, they completed five 30-minute training sessions on 5 consecutive days (Monday – Friday) at the university. Following training, they again completed the battery of cognitive and motor tasks at a post-test session soon after training (3/4 days) and a Retention session following a subsequent period of time (8-10 days) (see figure 3.2.2-1 for an outline of the experimental protocol). Both participants and researchers were blinded in this task. Participants were randomly allocated to one of two groups (training or control). The

participants were not aware that there was an alternative training condition. Group allocation was determined using a computer-generated random number sequence prepared by an investigator who was not involved in recruitment, intervention or data collection. Different researchers were involved in (a) carrying out pre-test, post-test and retention test sessions ("assessors") and (b) carrying out the intervention training sessions ("trainers"). The person carrying out the pre/post/retention assessments was naive as to the allocation of each participant to training condition.

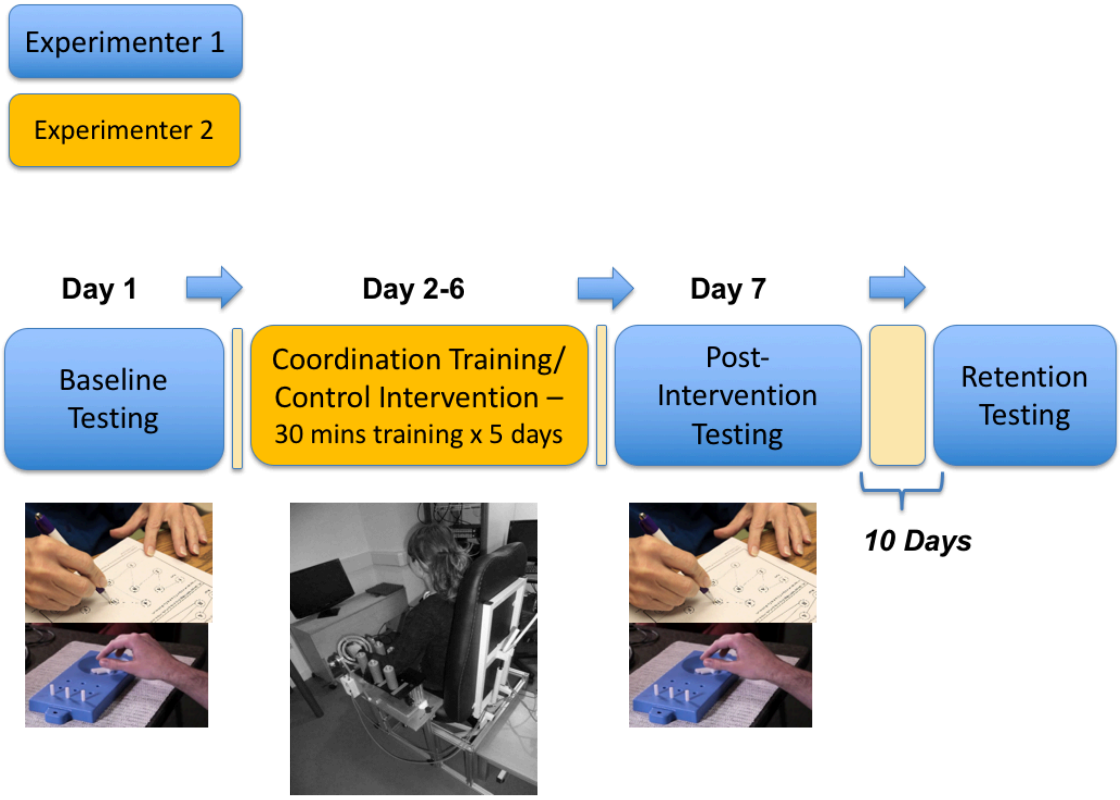

Figure 3.2.2-1 Schematic illustration of the experimental protocol. Assessors carried out the pre-test, post-test and retention-test sessions, and were blinded to the intervention condition of participants.

3.2.2.1 The Motor Training Intervention

On each of 5 training days (Monday-Friday), training group participants performed a motor training task using their Left limb only. The motor intervention comprised training on a centre-out target acquisition task. Participants had to acquire visual targets appearing on a screen in front of them using coordinated wrist movements (see Figure 3.2.2-2 below) as in Trial 1 (Chapter 2). However there was an important distinction: participants received no concurrent visual feedback of cursor position while executing movements, instead only receiving post-trial feedback of their cursor trajectory.

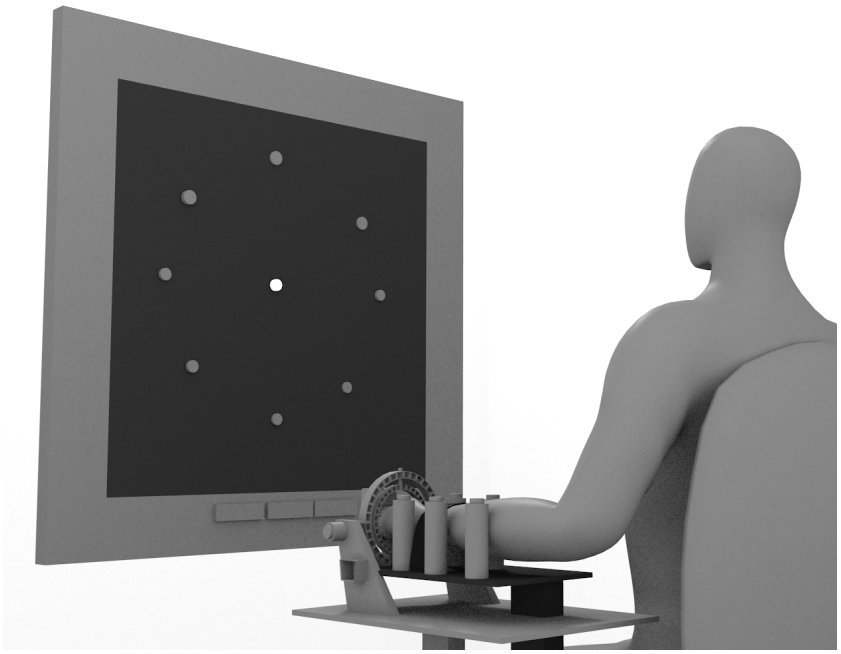

Figure 3.2.2-2 Experimental set-up. Participants were seated .75m from a visual display (not to scale), with their forearm secured in place to prevent lateral motion. Participants were strapped onto the manipulandum which controlled the position of the cursor onscreen. They were required to move their wrist in 2 degrees of freedom (flexion-extension and ulnar-radial deviation, or combinations of these movements) in order to hit one of eight targets appearing onscreen.

Participants were comfortably seated in an adjustable experimental chair positioned 0.75 m in front of a 24" computer screen, with the centre of the screen at eye level (Figure 3.2.2-2). Their upper limbs were supported on horizontal platforms, with lateral motion prevented by foam-covered posts placed on either side of each arm. The head, neck, torso and feet were also fully supported. The forearms were stabilised in mid-pronation and the elbows semi-flexed (100-120˚). Each hand was securely fixed within a manipulandum (Figure 3.2.2-3, Panel A) that was instrumented to transduce displacements of the wrist in two degrees of freedom (i.e. flexion-extension, and radial-ulnar deviation). The outputs from the transducers were low-pass (analog) filtered at 8Hz, and then sampled at 2000Hz. The transduced displacement of the wrist was projected onto the LED screen as a yellow cursor in the shape of a circle. The cursor responded to displacement of the wrist in an intuitive way such that extension of the right wrist, and flexion of the left wrist, would move the cursor to the right. For both limbs, radial deviation moved the cursor upwards, and so on.

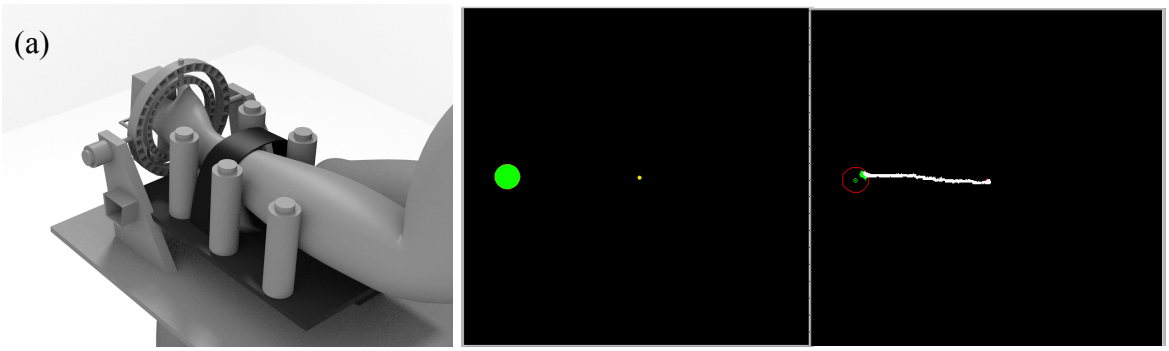

Figure 3.2.2-3 (a) A 2 Degree-of-Freedom Manipulandum was used to record wrist flexion & extension. The hand was positioned in the horizontal plane, with the fingers straightened in line with the palm. After holding the limb in 'neutral' position in the home position in the centre of the screen, a target would appear at one of 8 locations on the screen (b). Participants received no online visual feedback of their cursor position during movement, however they received post-trial visual feedback of their cursor trajectory (c).

The trial was initiated when participants held the cursor in a circular 'home' position in the centre of the screen for 50ms, which caused a target to appear (Figure 3.2.2-3 panel b). Participants received visual feedback of the cursor position whilst moving to the home position. Targets located at 45° intervals around the circumference of a circle defined by a radius corresponding to 15° of wrist displacement (8 distinct positions) were presented in pseudo-random order. The participant was instructed that following the presentation of a target, they should move the cursor to the target "as quickly and as accurately as possible", to emphasise equally the importance of both velocity and accuracy. Participants were instructed to attempt to hit the target on the first outward movement of their wrist, to prevent target acquisition strategies in which participants moved rapidly back and forth over the target space.

Participants received no visual feedback of the cursor position while moving towards the target, and were only provided with auditory feedback (a loud 'beep') if they successfully acquired the target. The trial ended once the target was hit, or, if participants were unable to hit the target, after 4 seconds elapsed ('timeout'). Following the trial, the cursor trajectory recorded for the duration of the trial (for the period of time between target presentation and acquisition or timeout) was presented onscreen for 4 seconds.

In each session, participants performed the task over 4 blocks of 32 trials. Blocks lasted 4 minutes, with a 1-minute break between blocks, thus training sessions lasted approximately 20 minutes per day. Task difficulty was increased incrementally over the course of the training period by manipulating the target size. The targets decreased in size progressively over the course of each training session, with the following day's session beginning on the final target size of the previous day. Targets decreased in size to the order of 1 mm per block over the course of 4 blocks per day (3.75 x 3.75 pixels on

screen resolution of 96DPI) (Table 3.2-1). An additional fifth block of the movement task was carried out on Day 5 of training, however the target size was increased back to the original size of the Day 1 Block 1 target (10° / diameter 20mm). This was in attempt to capture change in target acquisition percentage following the training period.

Table 3.2-1 Progression of target size over the intervention period.

Training Session	**Target Size in Degrees** *(corresponding diameter in mm)*				
Block	**1**	**2**	**3**	**4**	**5**
Day 1	10° (20mm)	9.5° (19mm)	9° (18mm)	8.5° (17mm)	-
Day 2	8.5° (17mm)	8° (16mm)	7.5° (15mm)	7° (14mm)	-
Day 3	7° (14mm)	6.5° (13mm)	6° (12mm)	5.5° (11mm)	-
Day 4	5.5° (11mm)	5° (10mm)	4.5° (9mm)	4° (8mm)	-
Day 5	4° (8mm)	3.5° (7mm)	3° (6mm)	2.5° (5mm)	**10° (20mm)**

3.2.2.2 The Active Control Task

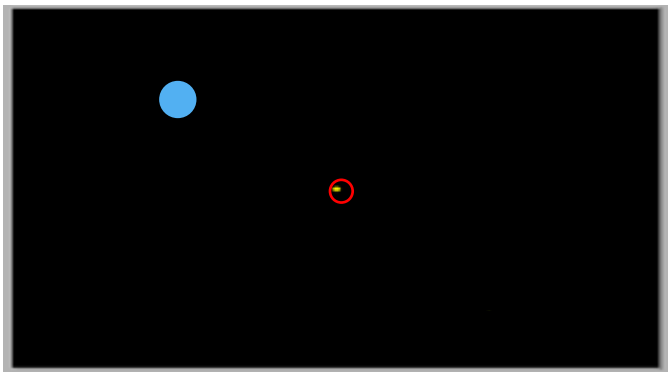

Figure 3.2.2-4- The active control task. The active control task closely resembled the visual display in the motor training task, however, participants were not required to make wrist movements to hit the target. They simply had to count how many blue targets appeared. Target size diminished as in the motor training task.

The control task schedule was identical to that of the motor training group, consisting of 4x4-minute blocks of training held on 5 consecutive days. The settings were also identical to that used for motor training, with participants sitting in the same chair and identical targets appearing onscreen - in order to keep attentional demands consistent across groups. However, limb movements were not required in the control task. Each of the 8 targets appeared four times (in pseudo-random order) in each block of 32 trials. The participants were asked to count the number of instances that a target was blue in colour (the frequency of blue target occurrence was varied randomly between 4-9 times per block, Figure 3.2.2-4). Participants were asked for the total after each block, and

given verbal feedback on their performance with a view to keeping them engaged in the task. Over the course of the 5 training sessions, the size of the targets was decreased progressively during the course of each block, using the schedule described for the motor training condition. The target size progression was identical to that used in the motor training condition (Table 3.2-1). The intent was to increase task difficulty in precisely the manner of the motor training task.

3.2.2.3 Pre- and Post-Training Motor Assessments

The pre-, post- and retention training motor assessments comprised a centre-out target acquisition task. A circular "home position" was presented in the centre of the screen. The participant was instructed to move the cursor into this central circle in order to begin each trial. Holding the cursor in the central circle for 50ms caused a target to appear. Targets located at 45° intervals around the circumference of a circle defined by a radius corresponding to 15° of wrist displacement (8 distinct positions) were presented in pseudo-random order. For example, acquisition of target position 3 required that 15° of radial deviation be produced in combination with 15° wrist flexion. The participant was instructed that following the presentation of a target, they should move the cursor to the target "as quickly and as accurately as possible". There was continuous (i.e. concurrent) visual feedback of cursor position. If the cursor reached the target region (10% of distance from the origin to the centre of the target), and was then maintained continuously within this region for 50ms, a tone (60ms, 900-Hz sinusoid) signalled successful target acquisition. At this time both the cursor and the target were extinguished. In the event that a target was not acquired within a period of 4 seconds following its presentation, the target was extinguished and the screen refreshed. The participant was asked to relax following each trial - in order to return the cursor to the home zone (i.e. the wrist in a neutral position). The next target appeared 2–3 s later. Custom Labview (National Instruments, Austin, TX) programmes were used to implement all procedures for stimulus presentation and data collection.

The right (transfer) limb was always assessed before the left (training) limb. Prior to the initial pre-training assessment, the participant undertook eight practice trials (one to each target position), first with the right limb and then with the left limb. In each of the subsequent assessments, each limb was employed in four blocks of 32 trials (128 trials in total for each limb). Within a block, each target appeared on four occasions. The duration of each block was approximately four minutes. There was a rest period of approximately 1 minute between successive blocks. The total duration of each assessment session was about 40 minutes.

3.2.3 Assessments

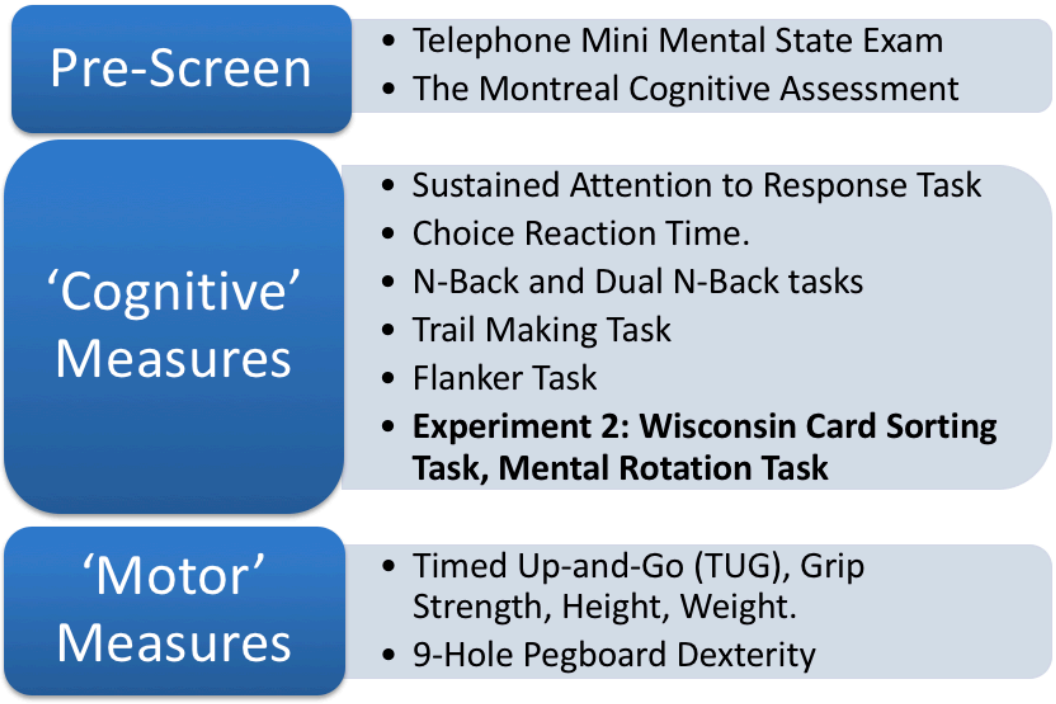

Figure 3.2-2 A list of the measures used at pre-screen, and at the baseline, post-intervention and retention sessions. The cognitive tasks used were identical to those used in experiment 1, with the addition of two additional tasks: the Wisconsin Card Sorting Task and the Mental Rotation Task.

In addition to assessment of performance on the baseline visuomotor task, all participants completed a battery of cognitive and physical function tests before (pre) and after (post) training, and again approximately 10 days after their post-training session (retention session). In the initial (pre) session, additional measures were carried out to measure mobility and cognitive impairment. The Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) was designed as a rapid screening instrument for mild cognitive dysfunction. Handedness was measured using the Edinburgh Handedness Inventory (Oldfield, 1978). The Timed Up and Go task (Podsiadlo & Richardson, 1991) was used to assess mobility. The participants were required to stand from a seated position, walk three metres to a line marked on the floor, turn around and walk back to the chair and sit down again. The researcher obtained the time taken to complete the task using a stopwatch. Anthropometric measurements were also taken, consisting of participant height (cm) and weight (kg) measured using a Salter electronic scales. Body-mass index was calculated from these measures (kilogram/metres squared).

3.3 Tests of Cognitive Function

A Sony Vaio 15-inch laptop was used to run the battery of cognitive tests. Computer-based tasks were programmed using E-Prime 2.0, and PEBL (Psychology Experiment Builder Language, Mueller 2014). Responses were collected using a PST Serial Response Box, computer mouse and the laptop keyboard with modified buttons.

Cognitive tests identical to those used in Experiment 1 (Section 2.2.4) were again repeated in the pre, post and retention sessions (listed below). However, two additional tasks were included in this experiment. These were computerised versions of the Mental Rotation Task and the Wisconsin Card Sorting Task. These tasks are outlined below. They were included as additional measures of executive function, with a view to ensuring that the battery of tests provided the widest possible coverage of key domains (e.g. Diamond & Ling, 2016; Papp, Walsh & Snyder, 2009; Moreau, Kirk & Waldie, 2016). In Experiment 1, no measure of mental rotation was included. Similarly, although the TMT was included as a test of cognitive flexibility and global executive function, the WCST was included as an additional measure of these capabilities.

Table 3.2-2 Cognitive measures and the corresponding underlying executive function measured in the task.

Task	Executive Function Domain
Flanker Task	Inhibitory control/response inhibition
Choice Reaction Time Task (CRT)	Processing speed, reaction time
n-Back and Dual n-Back Task	Working memory
Trail Making Task (TMT)	Cognitive flexibility, task switching/ set-shifting; visual search; motor speed; processing speed.
Sustained Attention to Response Task (SART)	Sustained attention, inhibitory control/ response inhibition.
Mental Rotation Task	Mental rotation ability, spatial working memory
Wisconsin Card Sorting Task	Cognitive flexibility, global executive function, working memory.

These tasks were carried out in a consistent order. In all cases, however, alternate versions of the tasks (e.g. randomised order of stimuli presentation and/or stimuli) were used in attempt to minimise practice effects (Benedict & Zgaljardic, 1998).

3.3.1.1 Mental Rotation Task:

Summary

In experiment 2, we used a computerised version of a mental rotation task derived from Shepard and Metzler's original cube rotation task (1971) using 2-dimensional images. The experimental task required that the participant indicate as quickly as possible (by pressing a button) whether the two objects depicted were identical (and rotated relative to one another), or were mirror images. Participants were presented with two shapes on the computer screen and had to press either a keyboard button labelled "Same" if the shapes could be rotated in order to appear identical, or a button labelled "Different" if the shape on the right was a mirror image of the figure on the left. Two different stimuli shapes were used: an "L" shape and a "bolt" shape. It has previously been shown that adults have a greater facility to mentally rotate familiar shapes than unfamiliar shapes. It was thus hypothesised that decisions made following of presentation of the L shape would be made more rapidly than when the bolt shape was displayed.

Participants were instructed to respond as quickly and as accurately as possible. The stimuli remained onscreen until a response had been made. Upon responding, participants were immediately presented with the next pair of shapes. Participants carried out 32 trials. These consisted of "Same" or "Different" trials in equal measure. There were possible 5 different degrees of rotation of the second shape relative to the first shape presented: 0 degrees, 45 degrees, 90 degrees, 135 degrees and 180 degrees. Typically reaction times increases linearly with the angle of rotation (Georgopoulos & Massey, 1987). The order of stimulus presentation was pseudo-randomised.

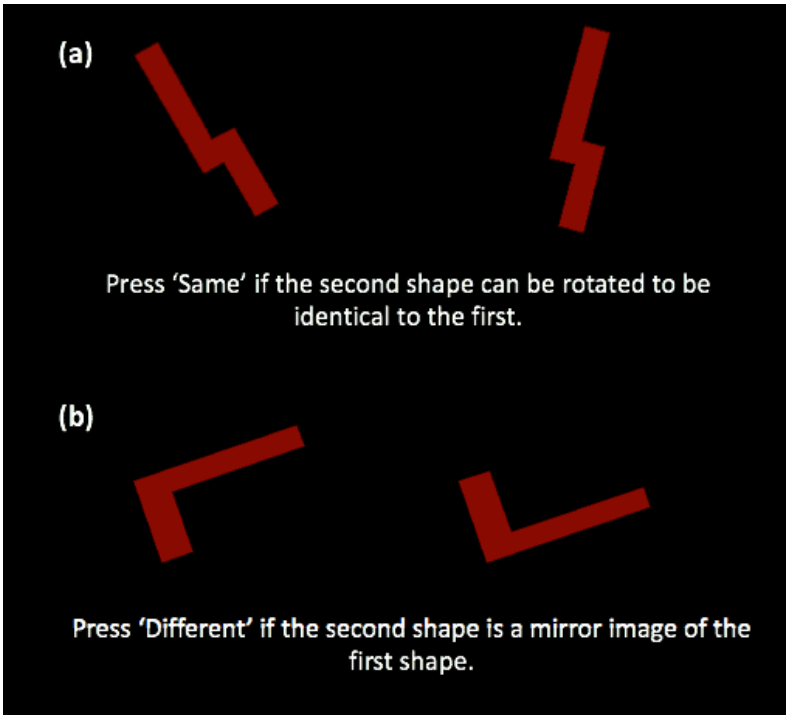

Figure 3.2-4 Example of the stimuli used in the Mental Rotation Task. (a) Depicts an example of the 'Z-bolt' stimuli. In this example, participants would correctly respond by pressing the 'Same' button, as the second shape can be rotated clockwise or anti-clockwise to be identical to the first. (b) Depicts an example of the second class of stimuli: the 'big-L' stimulus. In this example, participants would correctly respond by pressing the 'Different' button, as the second shape is a mirror image of the first shape, and cannot be rotated clockwise or anti-clockwise to match the first shape.

Outcome measures:

Reaction time (RT) was the primary outcome measure. Median RT scores were obtained separately for the different conditions of the target stimuli (e.g. 0° rotation, 45° rotation, 90° rotation, 135° rotation and 180° rotation) for each participant.

3.3.1.2 Wisconsin Card Sort Task

Summary

The WCST is ostensibly a measure of set-shifting, attention, working memory and visual processing ability. It was developed to assess abstract reasoning, and an ability to shift cognitive strategies in response to environmental changes (the changing rules of the task). Researchers have found that task performance on the WCST in impaired in people with damaged prefrontal cortices (Milner, 1963; Nelson, 1976; Stuss et al., 2000) and basal ganglia (i.e. patients with Parkinson's disease; Lees and Smith, 1983; Gotham et al., 1988). A meta-analytic review (Rhodes, 2004) found robust performance deficits among older adults in the number of categories achieved and perseverative errors committed in the WCST. It has been suggested that these age effects resemble the effects of prefrontal lesions on WCST performance (Rhodes, 2004; Head, Kennedy, Rodrigue

& Raz; 2009) and studies have found associations between lower PFC volume and increased perseveration in older adults (Head et al., 2009). However, Nyhus and Barceló (2009) reviewed the clinical and brain imaging research pertaining to WCST performance, and concluded that attempts to localise brain regions associated with WCST performance were ill-devised, as performance engages a widely distributed brain network, consisting of cortical and subcortical regions carrying out integrated functions. In additional support for these findings, they found that WCST performance does not distinguish between prefrontal and non-frontal lesions.

Task Outline

The test involves the use of 4 stimulus cards and one response card (for each trial)- shown in various forms, colours and numbers (three possible sorting criteria). Four cards are displayed on the top of the screen and one at the bottom, the participant is required to match this bottom card to one of the top cards based on the sorting principle (by shape type, by colour, or by the number of shapes shown on the card). Throughout the test, there are unannounced shifts in the sorting principle. This requires that the participant integrates the new information and shifts their approach to sorting accordingly. Feedback is given immediately after each attempt to sort a card (CORRECT or INCORRECT flashes onscreen).

In this task we used the shortened WCST-64 version (Haaland et al., 1987). This version uses only the first 64 WCST cards of the deck - which significantly reduces administration time. Although adoption of this version is relatively recent (first use by Haaland et al, 1987), the results obtained are generally comparable those derived from the standard 128 card version. The two forms of the test are equivalently sensitive to the effects of both normal and pathological ageing (Wagner & Trentini, 2009). We used a computerized version of this task as a means of facilitating data collection (perseveration errors are discriminated from non-perseveration errors and total errors, etc).

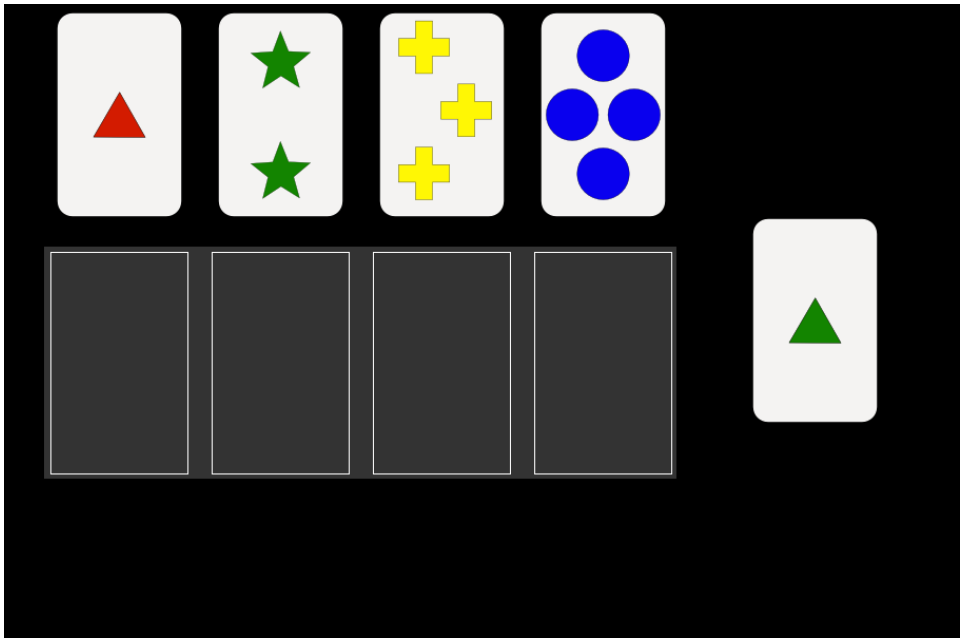

Figure 3.2-5 The starting screen in the Wisconsin Card Sorting Task. Participants were required to match the card from the deck on the right lower corner of the screen to one of the four cards at the top of the screen, which remained the same throughout the task. The cards can be matched according to the shape (triangle, star, cross or circle), the colour (red, green, yellow or blue), or the number of shapes on the card (one, two, three or four). When a participant has selected their response, they will receive feedback on whether or not their response was correct. They must use this feedback to figure out the matching rule.

3.3.1.3 Outcome Variables:

Accuracy/ Error data are the most important outcome measures, as the task is not timed. Kongs, Thomson, Iverson, & Heaton, 2000, propose that total number of errors and conceptual level responses (CLRs) are working memory indices, whereas perseverative errors and perseverative responses measure cognitive flexibility. Following this interpretation, four types of errors are reported to measure performance:

1. **Total errors:** Total of all incorrect responses, i.e. the sum of perseverative, non-perseverative and unique errors (unique errors are errors where the stimulus card and the response card do not match on any dimension).
2. **Conceptual Level Responses:** shows only intentional right responses and excludes random "rights". It is a measure of correct responses that occur in runs of three or more - the proportion of consecutive correct responses occurring in runs of 3 or more, reflecting insight into the correct sorting principles. Conceptual level responses are the number of correct responses that occur in runs of three or more divided by the number of trials then multiplied by 100.
3. **Perseveration errors**: Errors occurring when the participant incorrectly chooses the same rule for their choice as the previous incorrect choice.

4. **Perseverative responses:** Perseverative responses are the number of incorrect responses occurring when participants keep incorrectly applying the ‘old’ rule that would have been correct for the previous category.

3.4 Physical Measurements

Grip strength of both hands was measured using a digital hand dynamometer (Jamar). After a practice demonstration, participants were instructed to squeeze the handle of the dynamometer as hard as possible, and then over 3 seconds were instructed to increase force in order to ensure maximal force was recorded. Participants carried out the task with their left hand first, followed by the right (dominant) limb. The maximum value obtained across all three sessions (pre/post/retention) was used as a measure of maximum Grip Strength.

Dexterity was measured using the 9 Hole Pegboard Task (Rolyan® 9-Hole Peg Test), in which participants were instructed to place pegs one-by-one from the dish into 9 holes, then immediately replace them in the dish. Participants were given a practice trial on both hands before being timed completing the task as quickly as possible with each hand. All participants carried out the task with their right hand first, followed by left.

3.5 Statistical Analyses

All statistical analyses were carried out using R statistical software (R Core Team, 2012). A Bayesian re-sampling (bootstrapping) approach was employed to obtain estimates of the parameter values. Traditional frequentist approaches to parametric significance testing generate hypothetical sampling distributions from the null hypothesis, sampled according to the same stopping intentions as the collected data (Kruschke, 2013; 2014) in order to assess the probability that the fictitious data would be more extreme than the observed data. Typically, a p-value is defined as 'the probability of finding the observed data in the null hypothesis were true. Put differently, the *p*-value is "the probability that fictional, counterfactual data from the null hypothesis would be more extreme than the observed data, when those data were sampled and tested as intended by the current researchers" (Kruschke & Liddell, 2017, p.5). Thus, rather than relying on a hypothetical extreme distribution, Bayesian approaches rely on *intervals* based on prior theory and the observed data. Therefore a Bayesian approach, based directly on posterior credible intervals, is more intuitive and more credible (Kruschke, 2014).

Bootstrapping is a method of estimating the precision of parameter variables (i.e. parameter values that mathematically describe the data, such as medians, means, variances, etc.) by drawing randomly with replacement from an approximating distribution. Bayesian approaches to re-sampling use only the observed data in their parameter estimates. They create new datasets by reallocating or 're-weighting' the initial data, with Bayesian analysis providing the mathematical formula for the reallocation. Bayesian analysis gives us an explicit distribution of credibilities of the parameter values across the range of possible values. Initially, we begin with a prior distribution of the parameter values, based on prior knowledge, and then consider the new data we have collected in order to arrive at a posterior distribution of the parameter values. If there is no prior knowledge, un-informative prior distributions can be specified that have little influence on the posterior distribution. The posterior distribution assigns greater credibility to values that are consistent with the data (Krusckhe & Liddell, 2017). This posterior distribution gives us the credibility of every single parameter value, and can indicate which parameter values are most credible (i.e. the mode of the distribution). It also gives us the range of parameter values that cover the most credible set of values (known as the 'Highest Density Interval', or HDI). For example, if the 95% HDI

indicates that most credible values of the mean, μ, lie between 10 and 15, then we would state a belief that the mean μ has 95% probability of falling between 10 and 15.

For a given parameter, the posterior distribution can be approximated using re-sampling techniques. Markov chain Monte Carlo (MCMC) is a method of sampling probability distributions that can generate confidence (credible) intervals when assumptions of normality are violated. Measuring the properties of a target distribution by generating samples of representative random values from the distribution is called Monte Carlo simulation. A Markov chain is a 'directed random walk' through a parameter space that includes all the possible values of the parameter we are interested in. The term random walk indicates that each step in the parameter space is independent of the previous steps. A chain of such steps, in which the current step has no memory for previous states, is called a Markov Chain. The term 'directed' is used to imply that although the next value in the chain is selected at random, some values are more likely to be drawn than others, in proportion to their probability (which is determined by both the data and the prior distribution) (Hamra, MacLehose, & Richardson, 2013). In other words, the chain is more likely to 'walk around' more important areas of the parameter space. We can thus reconstruct the distributions of the parameter, and these sample distributions mimic samples from the true posterior. The Central Limit Theorem dictates that with sufficient resampling, Monte Carlo estimates approach normality, regardless of the distribution characteristics of the original sample. Additional benefits of this approach are that they do not require equal group size, are less adversely affected by missing data and can be used with data that are not normally distributed.

The analysis was implemented in R using the MCMCglmm package (Hadfield 2010) to fit Generalised Linear mixed models using Markov Chain Monte Carlo techniques. An unspecified variance–covariance matrix was used for random effects and residuals, to allow unconstrained correlations in the random effects and residuals. As we had no prior information about the covariance matrix in advance of analysis, weakly informative inverse Wishart priors were used for the random and fixed effects. These priors should have a minimal influence on the posterior distribution. For all cognitive outcomes measures, 100,000 iterations (samples) of the model were undertaken. The size of the sample should be such that the estimates are accurate and stable (Kruschke, 2014), i.e. if the MCMC analysis was run again, the 95% HDI should not be much different. The 'thinning interval' was set at 10. The thinning interval is a method of reducing the chance of autocorrelation among iterations. The thinning interval specifies the MCMCglmm procedure to only keep every 10^{th} value in the sampling process, in order

to reduce autocorrelation, as samples that are near each other in the sampling process are more likely to be correlated. The 'burn-in' period, which instructs the procedure to ignore the initial samples, was set to 10,000. This is important as we do not want the sample to be unduly influenced by the random starting point of the Markov chain. The resulting effective sample size was 9,000 for each parameter.

Model Diagnostics: The mathematics of MCMC imply that infinitely long chains of samples will attain perfect representations of the posterior distributions, however due to limited time and computer memory, a sample size must be decided upon. Thus, the quality of our infinite MCMC chain must be checked for signs of unrepresentativeness or instability. A number of steps were taken to assess the stability and adequacy of the obtained posterior distributions. One method is to run the MCMC analysis with different starting points, and the resulting chains should 'converge' with or overlap each other. Visual inspection of trace and density plots were examined to assess convergence. In addition, Gelman and Rubin diagnostics (Gelman & Rubin, 1992) were run to obtain the Potential Scale Reduction (PSR) factor to ensure 'convergence' was achieved within each model. The PSR is a numerical check of the variance between chains, with values near 1 indicating adequate convergence.

Planned Contrasts: Scores obtained prior to the intervention (pre), following the intervention (post) and at a retention session following a period of no training (ret) were compared for all cognitive outcome variables, and the results of planned contrasts were summarised using least-square means tables. Least square means and pairwise contrasts for the MCMCglmm model were calculated using the lsmeans() package (Lenth & Hervé, 2015). Corrections for multiple comparisons were not necessary, as by utilising Bayesian analyses, we are not basing our decisions on error control or sampling distributions, but on the properties of the posterior distributions of the parameter values (Krushcke and Liddell, 2017). We are making direct comparisons between two sets of data, and the use of multilevel models allows us to capture the common influences. In addition, the prior distribution regulates any point estimates. In all cases, separate analyses were carried out for the intervention (Motor Training) and active control (Control) groups.

3.5.1 Effect Size Estimates

Cohen's *f* was calculated as a measure of effect size for each of the planned contrasts (Cohen, 1988). Cohen suggested that *f* values of 0.1 indicate a small effect size, values of 0.25 indicate a medium effect size, values of 0.4 or over are indicative of a large effect size. This standardized measure of effect size allows us to compare the effects of the different conditions on the different outcome measures and assists in the interpretation of the p-value.

3.5.2 Model fitting: Deviance Information Criterion

The Deviance Information Criterion (DIC) was utilised as a method of Bayesian model comparison. Models with smaller DIC are better supported by the data, and thus all models used herein were selected on the basis of having an optimal DIC (see Chapter 2 section (Section 2.4.2) for a more detailed overview of DIC).

3.5.3 Dealing with outliers: Adjusted boxplots

In order to visualize the distribution of the data and identify any outliers, an adjusted version of the boxplot is used that is suitable for use with skewed data (Hubert and Vandervieren, 2008). In traditional boxplots, the whiskers are located at the points calculated using the following equations:

$$Q_1 - 1.5* \text{IQR} \quad \textit{(lower whisker)}$$
$$Q_3 + 1.5* \text{IQR} \quad \textit{(upper whisker)}$$

where IQR stands for the Inter Quartile Range, Q1 is the 25th percentile of the data, and Q3 is the 75th percentile of the data. Under this rule, anything lying outside the whiskers as a potential outlier. However, a weakness of this method is that as the length of the two whiskers are identical, it is only appropriate to use it when the distribution of the data between the two intervals is normally distributed. It is popular to overcome this shortcoming by transforming the data until it approximates a Gaussian distribution. However, this can cause problems for the interpretation of the data at later stages of the analysis. An alternative approach is to adjust the rule used to calculate the whiskers.

Adjusted boxplots include a measure of skewness in the equation, and allow the length of the whiskers to vary in line with the skewness of the data, using the following equation:

$$Q_1 - \exp(M, \alpha)1.5* \text{IQR} \quad \textit{(lower whisker)}$$
$$Q_3 + \exp(M, \beta)1.5* \text{IQR} \quad \textit{(upper whisker)}$$

where M is a measure of skewness (the authors suggest using the medcouple, a scaled median difference of the left and right half of the distribution), and α and β are scaling factors that determine the outlier boundaries, chosen to ensure that for skewed distributions without outliers, the probability of falling outside the whiskers is relatively small. In the present implementation, both were set to 1.5, indicating the whiskers extended to the most extreme data point which was no more than 1.5 times the IQR from the box. If the data is not skewed, then M is reduced to zero, and the classic equation is used.

3.5.4 Data Visualization with Pirate Plots:

Data is presented in figures using Pirate Plots. A pirate plot is a way of plotting data that shows critical distributional information about the data. Pirate plots, like traditional bar-charts, display central tendencies, but also include important information about the raw data and its distribution, which are hidden in traditional bar-charts. Please refer to Chapter 2 (section 2.4.4) for a more in-depth overview of Pirate Plots.

3.6 Cognitive Results

3.6.1 Summary

At the post-intervention testing session, changes were seen in performance on some measures of cognitive function (See Table 3.6-1 below for a simple visual summary). Changes were seen in performance on the Wisconsin Card Sorting Task (WCST) and the Mental Rotation task for the training group only at post-intervention, and both groups showed improvements on certain measures on the SART and n-Back tasks.

Table 3.6-1 Simple visual representation of changes in performance on the cognitive measures at the post-test session. The green arrow indicates improved performance, whereas the tilde indicates no reliable changes in performance were demonstrated.

Cognitive Test	Training Group	Control Group
SART Errors	↓	↓
CRT	~	~
Flanker	~	~
TMT	~	~
n-Back & Dual n-Back	↓ ~	↓ ~
WCST	↓	~
Mental Rotation	↓	~

- **WCST:** For the WCST, the training group exhibited improvements in both the number of conceptual level responses (CLRs) and the total errors at the post-test session, both thought to reflect aspects of working memory. No such reliable changes in performance were seen in the control group. This effect was also seen at the retention session.

- **Mental Rotation:** The Mental Rotation RTs improved for the training group only, both at post-test and at retention, although this change was accompanied by a small effect size.

- **Sustained Attention to Response Task:** For theSART, as in the first experiment, both groups reliably improved on the task by reducing the number of commission errors and omission errors made in comparison to the pre-test performance, both at post-test and at the retention session (although only a small effect was seen for both groups at retention for the number of omission errors).

- **nBack and Dual n-Back:** In the visuospatial n-Back task, control group participants exhibited improved accuracy performance on the 2-Back condition at post-test, and at retention both training and control groups showed an improvement in visual accuracy. For the Dual 2-back, the more difficult task, only the training group improved on 2-back visual accuracy post-test. This effect was not seen at retention. Improved performance on the most difficult task condition was only seen for the training group participants, and only in the visual accuracy condition.

No changes were seen in performance on the Trail Making Task, the Flanker task of the Choice Reaction Time task for either the control or training group across the post-intervention and retention sessions.

3.6.2 Montreal Cognitive Assessment (MoCA)

Participants scored an average of 27.27 on the MoCA, with Median score 27 and Standard deviation of 1.86. Scores ranged from 21-30. Using 23 as the cut-off score for potential mild cognitive impairment (as recommended by Carson, Leach & Murphy, 2017), two participants were identified as falling below the MoCA threshold, with scores of 20 and 21 (training group participants). These two participants were excluded from all further analysis.

3.6.3 Flanker Task

Data Cleaning:

The primary outcome variable, conflict cost, was calculated by subtracting the median congruent Reaction Time from the median incongruent reaction time. The adjusted boxplot method (Hubert and Vandervieran, 2008) was used to identify any outliers in the data. Three outliers were observed falling below the lower extreme whisker (conflict cost < -11.5): 2 in the control group (one in the post-test, one in the retention) and one in the training group (pre-test). One value fell above the upper extreme fence (conflict cost > 156), a pre-test in the control group. These four values were removed, and analysis was carried out on the remaining data.

Model:

In the MCMCglmm model, Time was included as a fixed effect, with Gender included as a covariate. Participants crossed with time (levels = pre, post, retention) was a designated random effect, and Age was included in the model as a covariate (random effect), as the DIC indicated better model fit including Age and Gender. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's f) were calculated.

Analysis:

While the Median conflict cost decreased more in the Training group (see Table 3.6-2), no evidence supported the conclusion that Motor Training had a reliable impact on performance of the flanker task. For all pre-post and pre-retention contrasts, no difference in pre-post session conflict cost score was seen for either the motor training group or the active control group.

Table 3.6-2 Pre-post contrasts for Conflict Costs

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	56.21(6.18)	52(6.02)	44.29(6.06)	0.459	0.10	57	0.038*	0.14	57
Control	53.20(5.30)	53.08(5.34)	55.28(5.31)	0.978	0.00	55	0.649	0.03	55

*indicates p-value <0.05

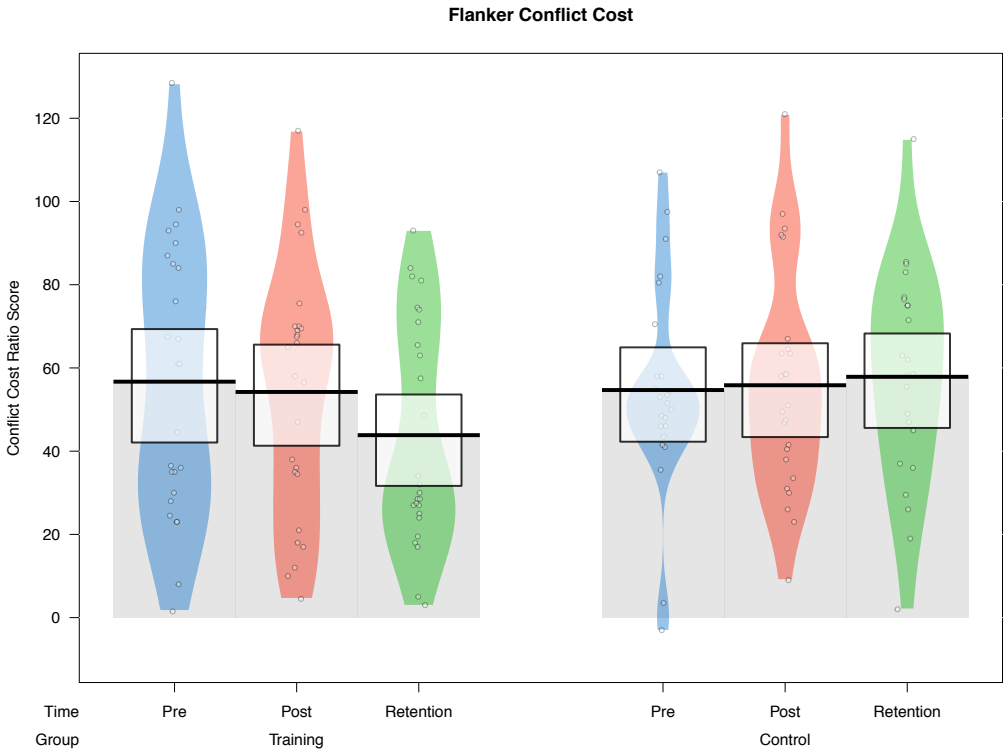

Figure 3.6-1 Changes in Flanker Conflict Cost scores across sessions for training and control groups. Conflict cost is the Median RT for incongruent trials minus the Median RT for congruent trials. For the training group, the most marked performance improvement is between pre and retention sessions. However, as the reliable intervals overlap somewhat, it is not possible to state that reliable and systematic improvements were observed after the motor training intervention. For the control group, the 95% Highest Density Intervals for sessions overlap substantially, indicating no differences in Conflict Cost scores across training session.

3.6.4 Choice Reaction Time Task

3.6.4.1 Cognitive Reaction Time

Cognitive Reaction Time scores were calculated as the median reaction time taken to release the Start button after the appearance of the Yes/No stimulus onscreen.

Data Cleaning:

Reaction time scores were removed if the response was inaccurate. Bounds were created using the adjusted boxplot method (Hubert and Vanderverian, 2008). Values falling outside of the extreme fences were classified as probable outliers. Adjusted boxplot method identified one value falling above the upper extreme fence (623 ms), originating from one control participant (pre-value). Eight values were identified as falling below the lower extreme fence (278ms); originating from 4 participants in the training group (three pre, two post, & three retention values). These values were removed prior to further analysis.

Model:

In the MCMCglmm model, Time and Target (levels = yes, no) were included as fixed effects, with Gender included as a covariate. Participants crossed with time (levels = pre, post, retention) was a designated random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the DIC. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's ***f***) were calculated.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups found no systematic changes in Cognitive Reaction Time for pre-post contrasts for either the training or control groups. Similarly, no reliable changes were observed in the pre-retention contrasts.

Table 3.6-3. Pre-post contrasts for the median Cognitive Reaction Times (ms)

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	454(19.2)	458(19.5)	440(19.4)	0.666	0.05	78	0.133	0.09	78
Control	475 (19)	469(19.2)	454(19.2)	0.560	0.06	79	0.063	0.11	79

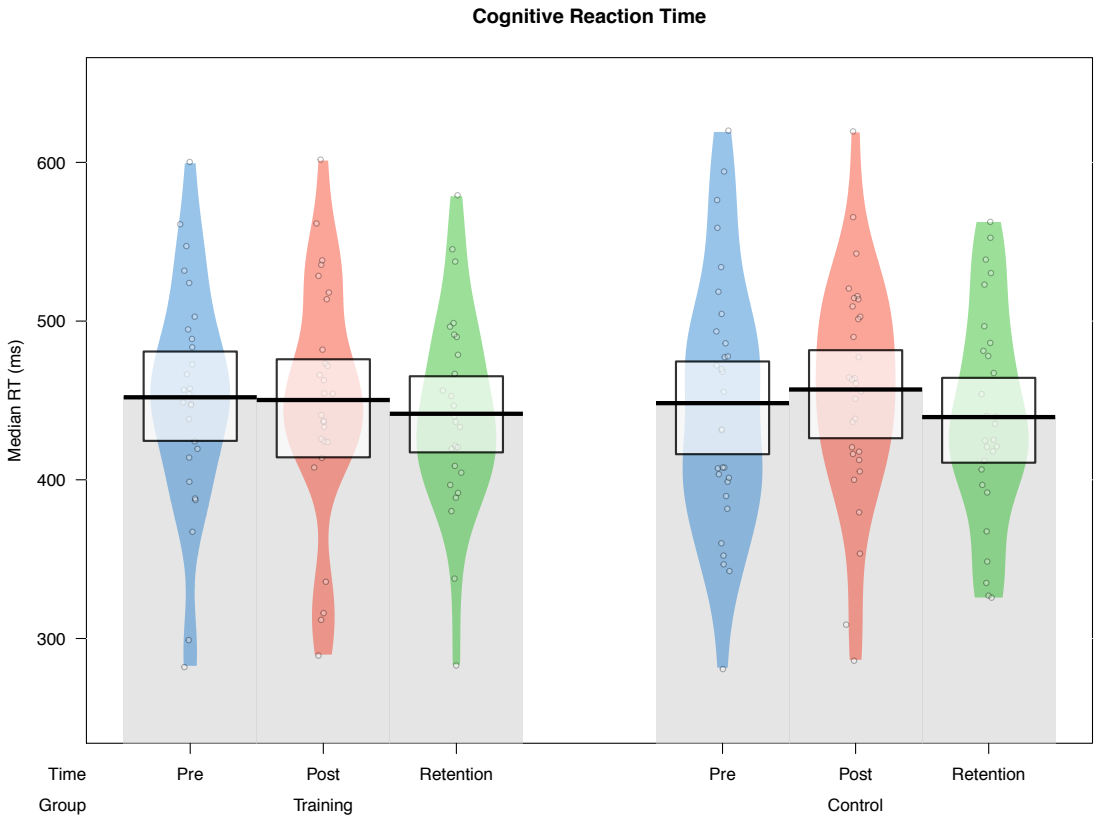

Figure 3.6-2 Pirate plot showing the Cognitive Reaction Times for Training and Control groups. For both the training and control groups, the 95% HDIs across all sessions overlap substantially, supporting the conclusion that no reliable changes were observed across sessions.

3.6.4.2 Motor Reaction Time

Data cleaning:

Adjusted boxplots revealed no outliers in the median Motor Reaction Time Scores for the training group. Adjusted boxplots revealed 6 values fell below the lower extreme fence of 159ms in the control group. All 6 values originated from one control participant, (two pre, two post, two retention values). These values were removed prior to further analysis.

Model:

In the MCMCglmm model, Time and Target (levels = yes, no) were included as fixed effects, with Gender included as a covariate. Participants crossed with time (levels = pre, post, retention) was a designated random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the DIC. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's ***f***) were calculated.

Analysis:

Data analysis found that there were no substantial differences in median motor RT at the post-intervention or at the retention session compared to the pre-test session for either the training group or the control group.

Table 3.6-1 Pre-post contrasts for the median Motor Reaction Time (ms)

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	360(33.5)	354(33.7)	325(34.1)	0.275	0.12	79	**0.014***	0.14	79
Control	349(30.6)	328(30.4)	315(30.7)	0.073	**0.20**	79	**0.007***	0.15	79

* indicates p<0.05. Medium and large effect sizes (Cohen's f >0.25) in bold.

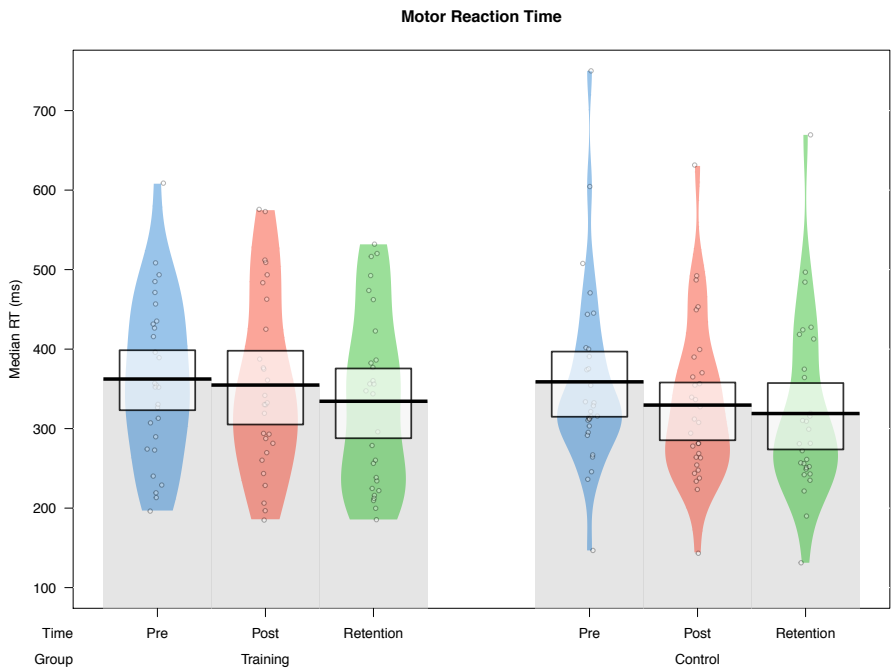

Figure 3.6-3 Pirate plot showing the median Motor Reaction Times for Training and Control Groups. Across all sessions for both the training and control groups, the 95% HDIs overlap substantially, indicating that no reliable differences were seen in median motor RT across sessions.

3.6.5 n-Back and Dual n-Back Tasks

Data Cleaning:

Reaction times below 150ms were excluded from RT data analysis. Incorrect responses were also removed from the RT data analysis. In the n-Back (single) task, results are reported separately for the 1-back and 2-back trials. In the dual task, Reaction Time data and Accuracy data were recorded separately for both visual and auditory stimuli, and for both 1-back and 2-back trials.

Adjusted boxplots found no outliers for any of the accuracy scores across auditory or visual domains. One value was removed from the Auditory Reaction Time scores as adjusted boxplots found it lay below the lower extreme fence of 630ms. This value originated from the control group (pre-test, dual task condition).

Model:

For all accuracy and RT outcome variables, the MCMCglmm model Time, n-back Task (levels= single, dual) and n-back Level (levels= 1-back, 2-back) were designated fixed effects. Gender was included as a covariate. We included Participants crossed with Time (levels = pre, post, retention) as a random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). Planned contrasts were carried out separately on the lsmeans for the different levels of n-back task and level. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's f) were calculated.

3.6.5.1 Accuracy

Accuracy scores were calculated for each of the four conditions, trial (1-back, 2-back) x stimulus type (auditory, visual) by subtracting the number of misses from the number of hits (Jaeggi et al., 2008); this is known as the discrimination index and gives a true value of performance.

Visual Accuracy: Visuospatial Task

For the visuospatial one-back task, accuracy scores at post-training or at the retention session were not systematically different from pre-test performance for either the training group or the control group. In the visuospatial 2-back condition, only the

control group accuracy scores were higher post-intervention (p=0.011, Cohen's *f*= 0.41). In addition, higher accuracy scores on the dual 2-back task were seen at retention compared to pre-test for both training (p=0.000, Cohen's *f* = 0.27) and control participants (p<0.000, Cohen's *f*= 0.34). Medians and standard errors can be seen in Table 3.6-4 below.

Visual Accuracy: Visuospatial (Single) Task

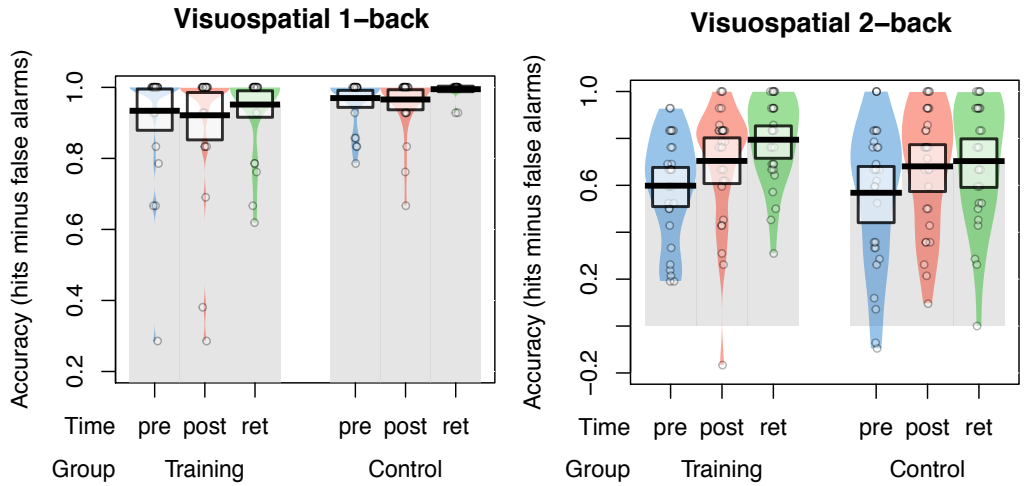

Figure 3.6-4 Pirate Plots showing the Visual Accuracy scores for Training and Control groups in the Visuospatial 1-back and 2-back tasks. Performance across groups was very high in the visuospatial 1-back, and no reliable differences can be observed across session for either the training or control groups. In the 2-back condition, for the training group, only the retention session accuracy scores are reliably higher than the pre-test session, with the 95% HDI falling completely above the pre-test interval. The post-test scores also appear to be higher than the pre-test scores. The 95% HDIs for the control group post-test and retention-test accuracy scores also fall above the pre-test 95% HDI, indicating improved accuracy performance on the task.

Visual Accuracy: Dual Task

For the dual one-back task, accuracy scores were higher at the post-training session for the training group, however this trend was only approaching conventional levels of statistical significance (p=0.086, Cohen's *f*= 0.28). No reliable systematic changes were observed across sessions for the control group.

In the most difficult task condition, the dual 2-back task, accuracy performance post-intervention was systematically higher for the training group, and this was accompanied by a medium effect size (p=0.012, Cohen's *f*= 0.32), however there was no difference in accuracy scores at retention compared to pre-test performance. Controls did not demonstrate any conventionally significant difference, or medium to large effect

sizes, across testing sessions. Means and standard errors can be seen in Table (3.6.4) below.

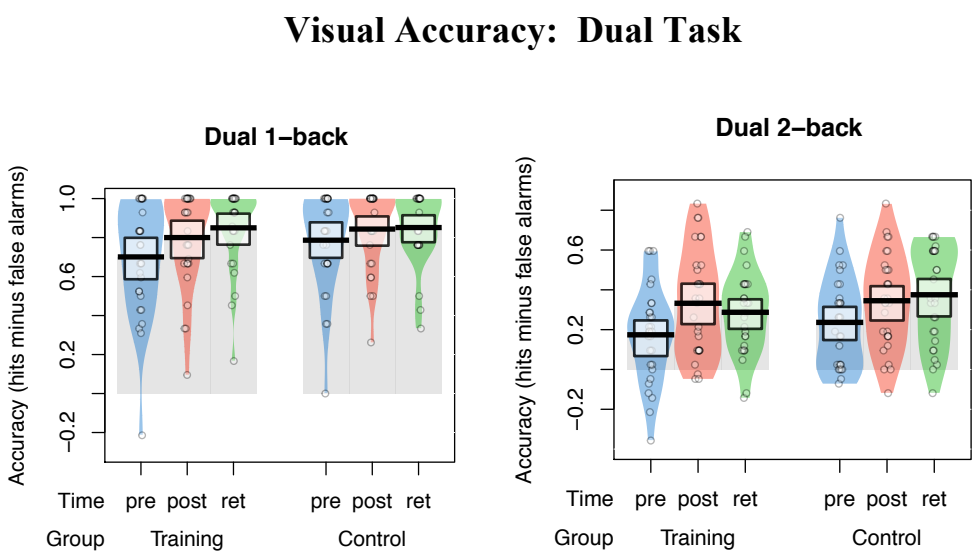

Figure 3.6-5 Pirate Plot showing the Visual Accuracy scores for Training and Control groups in the dual 1-back and dual 2-back tasks. In the dual 1-back, the majority of the training group 95% HDI in the post-test session falls above the pre-test interval, and the 95% HDI in the retention-test session falls predominantly above the pre-test interval, indicating improved accuracy performance at post and retention sessions. No reliable differences can be seen across dual 1-back sessions for the control group. In the 2-back condition (figure on the right), reliable improvements are seen for the training group, with the 95% HDI of the post- and retention sessions falling above the pre-test interval. For the controls, the majority of the 95% HDIs for the post- and retention-test accuracy scores fall above the pre-test 95% HDI, indicating improved accuracy performance.

Auditory Accuracy: Dual Task

For the 1-back task condition, no consistent changes in auditory accuracy were observed across sessions for either the training or control groups, and all effect sizes were small (Cohen's $f < 0.25$). Similarly, no consistent changes in 2-back auditory accuracy were seen across sessions for the training or control group.

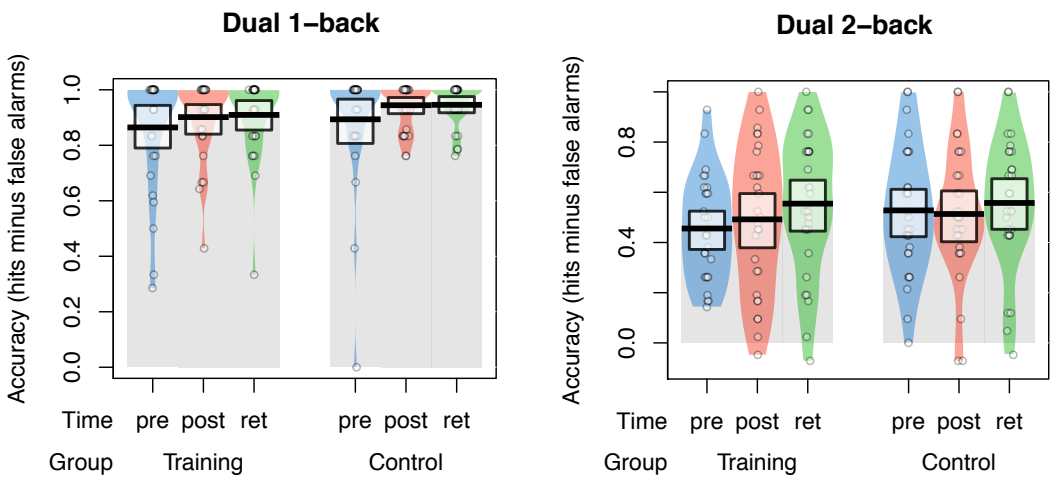

Figure 3.6-6 Pirate Plot showing the Auditory Accuracy scores for Training and Control groups in the dual 1-back and dual 2-back tasks. No reliable differences across session and group can be observed from the bean plots in the dual 1-back task condition. For the dual 2-back, the training group show higher accuracy scores at the retention session, with their 95% HDIs falling above the pre-test interval, indicating reliable performance improvements on the auditory accuracy measures.

Table 3.6-4 Visual Accuracy in the Visuospatial and Dual n-Back Tasks for Training and Control Participants.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Visuospatial	1	.933 (.054)	.917 (.054)	.946 (.055	0.761	0.06	39	0.813	0.04	39
		2	.577 (.054)	.665 (.054)	.793 (.054)	0.092	0.22	40	**0.000***	**0.27**	40
	Dual	1	.707 (.054)	.797 (.054)	.860 (.055)	0.086	0.28	40	**0.003***	**0.24**	40
		2	.209 (.057)	.352 (.055)	.267 (.056)	**0.012***	**0.32**	35	0.309	0.04	35
Control	Visuospatial	1	.965 (.051)	.966 (.051)	1.00 (.052)	0.984	0.01	39	0.410	0.15	39
		2	.554 (.052)	.668 (.051)	.752 (.052)	**0.011***	**0.41**	37	**0.000***	**0.34**	37
	Dual	1	.791 (.05)	.848 (.051)	.828 (.051)	0.193	0.21	40	0.407	0.06	40
		2	.302 (.054)	.311 (.053)	.366 (.053)	0.846	0.03	35	0.185	0.07	0.77

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

Table 3.6-5 Auditory Accuracy in the Dual n-Back Task for Training and Control Participants.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Dual	1	.864 (.045)	.902 (.045)	.911 (.045)	0.386	0.12	57	0.276	0.10	57
		2	.448 (.045)	.494 (.045)	.574 (.045)	0.307	0.11	57	0.005*	0.15	57
Control	Dual	1	.887 (.042)	.938 (.042)	.947 (.043)	0.277	0.20	57	0.207	0.10	57
		2	.557 (.043)	.532 (.044)	.559 (.043)	0.608	0.07	55	0.951	0.00	55

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

3.6.5.2 ***Reaction Time***

Visual Reaction Time: Visuospatial Task

No reliable systematic changes in visual RT performance in the visuospatial 1-back task were observed in either the training or control groups across pre-/post/retention-test sessions. Similarly, no differences in visual RT performance were seen across session and group in the visuospatial 2-back task.

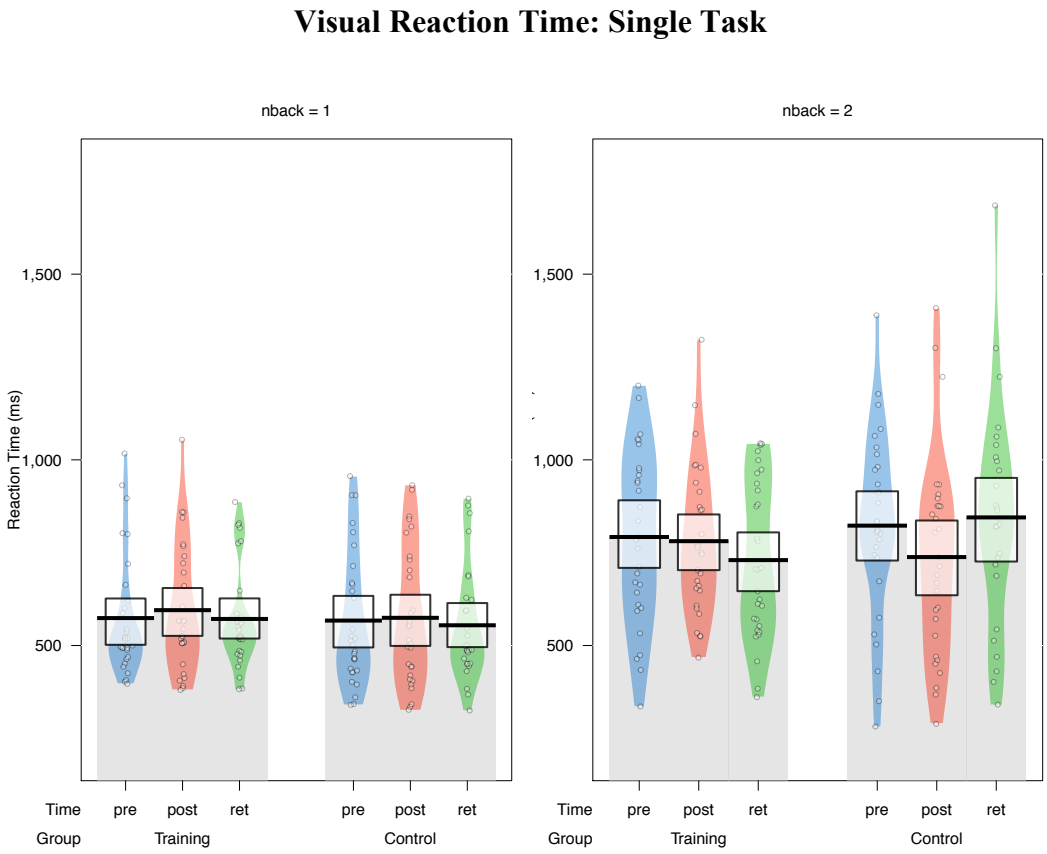

Figure 3.6-7 Pirate plot displaying the median Visual Reaction Time scores for the visuospatial 1-back and 2-back tasks. No reliable differences can be seen across session for either the training or control group in the 1-back task or the 2-back task.

Visual Reaction Time: Dual Task

In the dual 1-Back task, no systematic differences were observed between pre-test, post-test or retention-test visual RT performance for either the training or control groups. In the dual 2-back task, consistent reductions in RT were observed for the training group at post-test ($p=0.008$, Cohen's $f= 0.28$), and this effect was not seen at retention. No reliable differences in 2-back visual RT were observed across sessions for the control group. Medians and standard errors can be seen in Table (3.6-6) below.

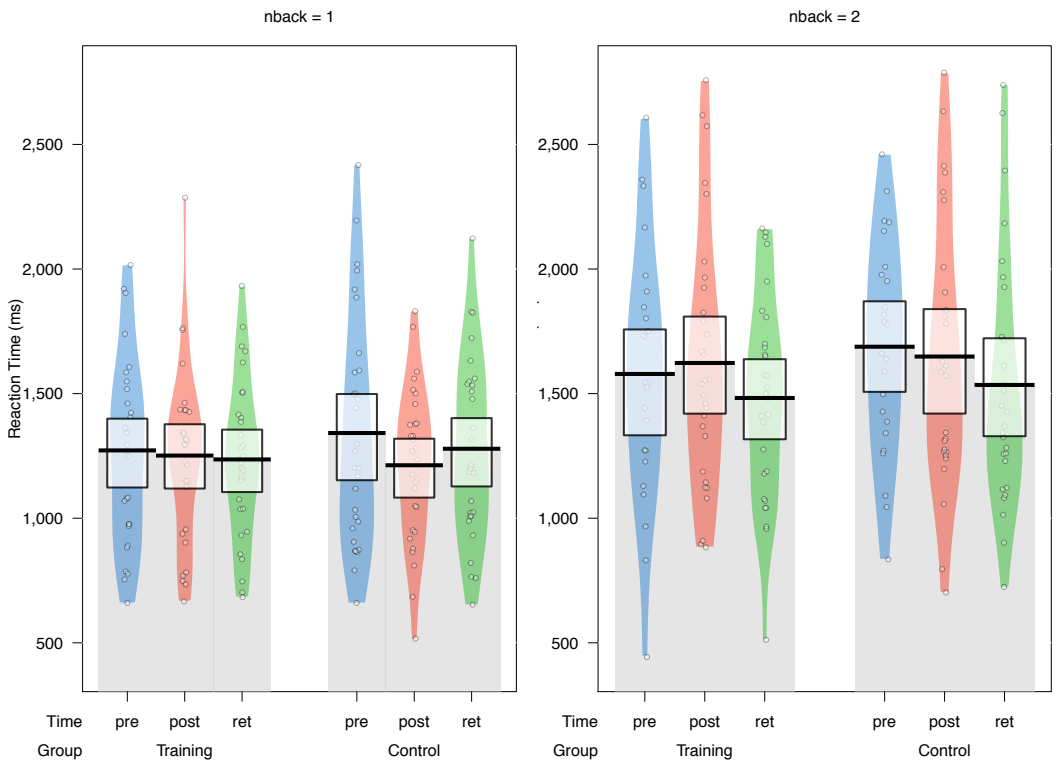

Figure 3.6-8 Pirate plot displaying the median Visual Reaction Time scores for the dual 1-back and dual 2-back tasks. No reliable changes can be observed across sessions for the 1-back or 2-back tasks in either the training or control groups.

Auditory Reaction Time: Dual Task

In the dual 1-back task, no reliable differences were seen in the 1-back task for either the training or control groups. Similarly, in the dual 2-back task, no systematic differences were observed across session in median auditory RTs in either control or training conditions.

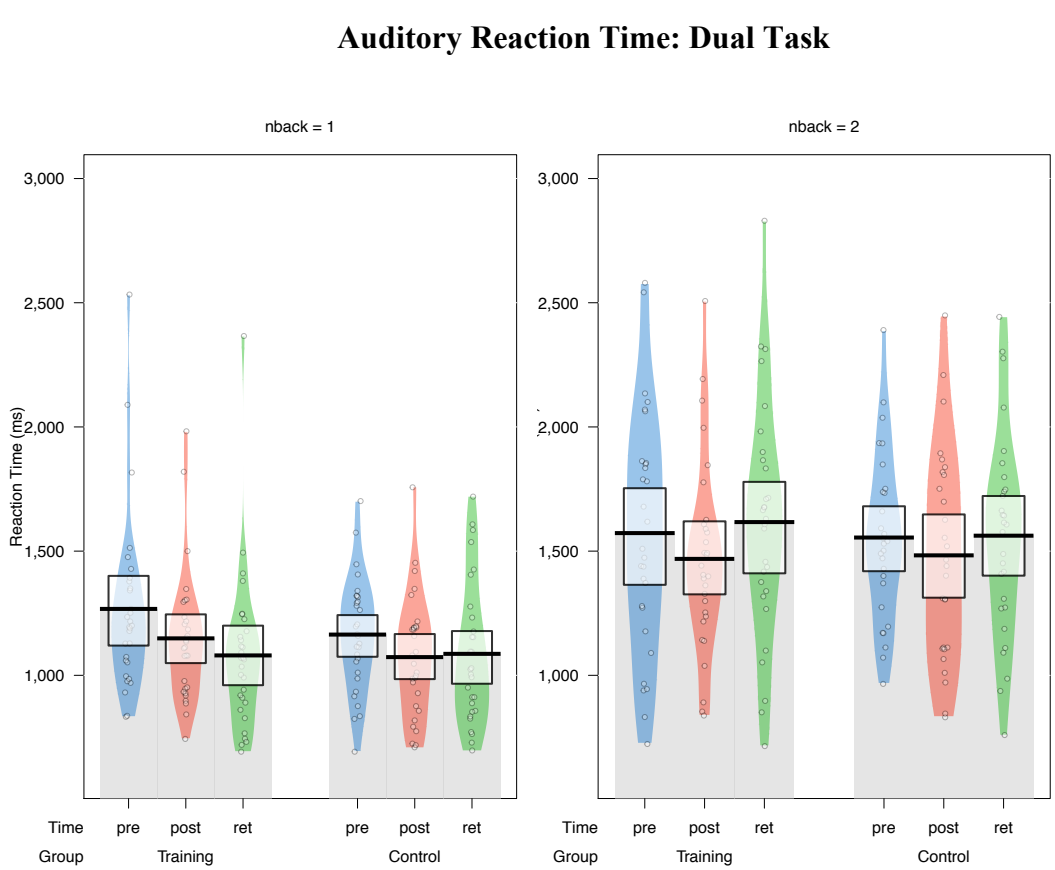

Figure 3.6-9 Pirate plot displaying the median Auditory Reaction Time scores for the dual 1-back and 2-back tasks. In the 1-back condition, the 95% HDI for the training group retention RT scores is credibly lower than the pre-test scores. No other reliable differences across session can be observed in the 1-back or 2-back conditions.

Table 3.6-6 Visual Reaction Time on the Visuospatial and Dual n-Back Tasks.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Visuospatial	1	585 (70.9)	607 (70.3)	587 (71.4)	0.793	0.13	39	0.978	0.01	39
		2	769 (72)	860 (71.2)	764 (70.3)	0.276	0.22	40	0.951	0.01	40
	Dual	1	1366 (71.6)	1312 (71)	1254 (70.6)	0.510	0.09	40	0.171	0.09	40
		2	1462 (76.6)	1699 (72.7)	1540 (73.4)	**0.008***	**0.28**	35	0.378	0.04	35
Control	Visuospatial	1	601 (80)	594 (81.3)	562 (82.6)	0.948	0.04	39	0.719	0.15	39
		2	827 (83.2)	769 (79.7)	861 (84.4)	0.600	0.12	38	0.762	0.04	38
	Dual	1	1318 (80)	1207 (81.8)	1289 (80.4)	0.309	0.15	40	0.788	0.02	40
		2	1737 (86.8)	1738 (84)	1514 (85)	0.995	0.00	36	0.056	0.11	36

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

Table 3.6-7 Auditory Reaction Time on the Dual n-Back Task.

			Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Task	***n-back***	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	Dual	1	1267 (74.9)	1149 (75)	1080 (74.2)	0.180	0.20	58	0.032*	0.15	58
		2	1584 (76)	1467 (73.9)	1609 (74.9)	0.187	0.14	57	0.779	0.02	57
Control	Dual	1	1165 (62.1)	1074 (62.1)	1088 (62.9)	0.236	0.19	57	0.322	0.08	57
		2	1560 (63.7)	1473 (65.3)	1564 (63.9)	0.279	0.11	55	0.954	0.00	55

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

3.6.6 Trail Making Task

Outcome measure:

In the Trail Making Task, participants carried out two Blocks of the TMT. Each block consisted of trial A and trial B, and participants carried out the tasks in an interleaved manner (i.e. trial order: A, B, A, B). Trial A consisted of numbers only (1-26), whereas Trial B consisted of numbers and letters (1-A-2-B etc.). The outcome variable was the median Reaction Time scores for Trial B divided by the median Reaction Time Score for Trial A; the 'B/A Ratio score'. Scores were calculated separately for each of the two blocks, but contrasts are reported on the combined results.

Data Cleaning:

Adjusted boxplots revealed nine values falling above the upper extreme fence (2.06); 8 in the control group (5 pre, 3 post) and one in the training group (pre). Three values were identified as falling below the lower extreme fence (0.84), one in the control group (pre-test) and two in the training group (1 pre-test, 1 post-test). Outliers were removed prior to further analysis.

Model:

In the MCMCglmm model, Time, and Block (levels = 1, 2) were designated fixed effects, with Gender included as a covariate. Participants crossed with Time (levels = pre, post, retention) were designated random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's f) were calculated.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups found that the ratio score increased across sessions for the training group. No reliable systematic changes in the TMT ratio scores across session were observed in the training or the control group.

Table 3.6-8 Changes in Trail Making Task Median B/A Ratio Scores

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	1.336 (.038)	1.248(.039)	1.246 (.038)	0.030*	0.19	139	0.024*	0.10	139
Control	1.308 (.049)	1.306 (.048)	1.312 (.048)	0.943	0.01	136	0.917	0.01	136

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

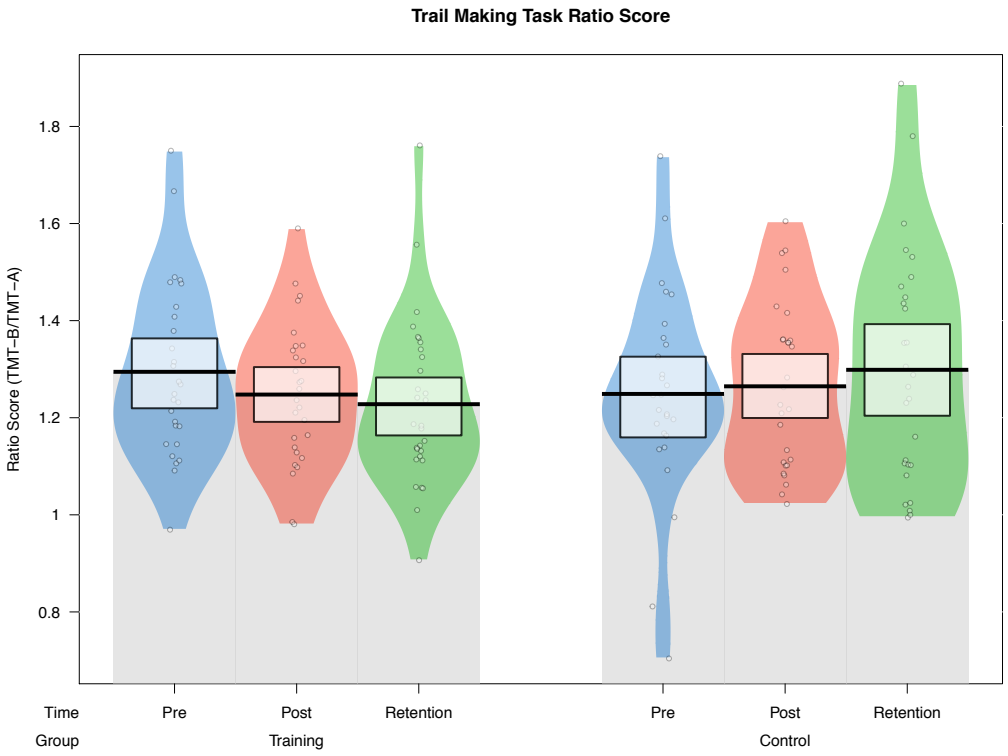

Figure 3.6-10 Pirate Plot showing the change in the B/A ratio scores across Session for Training and Control Groups. Lower ratio scores indicate better performance on the TMT. Ratio scores in the training group decrease across session, and increase across session in the control group, however no reliable differences in performance across time can be seen for either the training or control group.

3.6.7 Sustained Attention to Response Task (SART)

Two outcome variables for the SART were analysed, 'commission errors' and 'omission errors'. Commission errors are incorrect responses to 'NO-GO' trials, i.e. incorrectly pressing the mouse button in response to the number 3 stimulus. Omission errors are a failure to respond to 'GO' trials, i.e. failing to click the mouse button in response to numbers 1-2, 4-9. Both types of error purportedly reflect lapsing attention by indicating a break in task engagement. Commission errors are also said to reflect inhibitory control function, as participants have to withhold the automatic response (Manly, Robertson, Galloway & Hawkins, 1999).

Model:

For both outcome variables, the MCMCglmm model included Time as a designated fixed effect, and Gender was included as a covariate. Participants crossed with Time (levels = pre, post, retention) was included as a random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's ***f***) were calculated.

3.6.7.1 Omission Errors

Data Cleaning:

The adjusted boxplot method was used to identify any outliers. Five values were identified as falling above the upper extreme fence (46 errors). These values belonged to two control participants (2 pre, 2 post, 1 retention value) and were removed prior to further analysis.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups found the number of Omission errors was lower post-intervention for both the training group (p=0.012, Cohen's *f*=0.34) and control group (p=0.048, Cohen's *f*= 0.27). Both of these differences were associated with a medium effect size (Cohen's $f > 0.25$). At the retention session, no reliable changes were seen in the number of Omission Errors in comparison to the pre-test.

Table 3.6-9 Mean Omission Error Scores, and Pre-Post and Pre-Retention Session Contrasts.

Group	Pre	Post	Retention	Pre-Post contrasts			Pre-Retention contrasts		
	Mean (SE)	*Mean (SE)*	*Mean (SE)*	*p*	*f*	*df*	*p*	*f*	*df*
Training	6.36 (1.45)	3.88 (1.45)	2.94 (1.46)	**0.012***	**0.34**	54	**0.001***	**0.24**	54
Control	8.07 (1.93)	5.37 (1.90)	3.96 (1.94)	**0.048***	**0.27**	54	0.003*	0.20	54

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

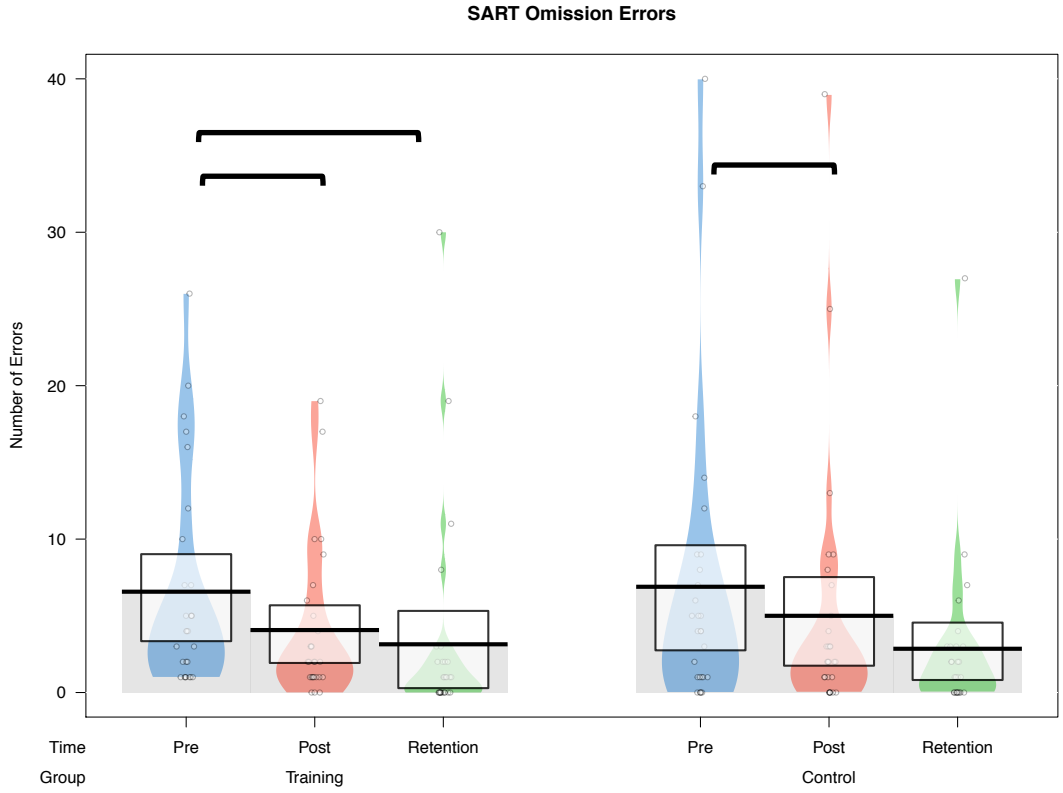

Figure 3.6-11 Pirate plot indicating numbers of omission errors made across sessions for the training and control groups. For the training group, the 95% HDI at the post-test falls below the interval for the pre-test session, indicating a high probability that Error scores were reliably lower post-intervention. In the control group post session, the 95% HDI falls largely within the pre-test interval, indicating no reliable difference was observed.

3.6.7.2 Commission Errors

Data Cleaning:

No outliers were identified using the adjusted boxplots method.

Analysis:

Planned contrasts looking at pairwise comparisons across time for both groups found the number of commission errors was lower for both the training group ($p<0.000$, Cohen's $f= 0.78$) and the control group ($p=0.000$, Cohen's $f= 0.72$) post-intervention, and these were designated large effects. Similarly, scores remained markedly lower at the retention session for both the training group ($p<0.000$, Cohen's $f= 0.35$) and controls ($p<0.000$, Cohen's $f= 0.32$), however a medium effect size was observed at retention.

Table 3.6-10 Mean Commission Error Scores, and Pre-Post and Pre-Retention Session Contrasts.

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	4.03 (0.57)	2.18 (0.56)	1.61 (0.57)	**0.002***	**0.44**	54	**0.000***	**0.28**	54
Control	3.47 (0.73)	2.34 (0.74)	1.55 (0.75)	**0.021***	**0.31**	57	**0.000***	**0.26**	57

* indicates $p<0.05$. Medium and large effect sizes (Cohen's f >0.25) in bold.

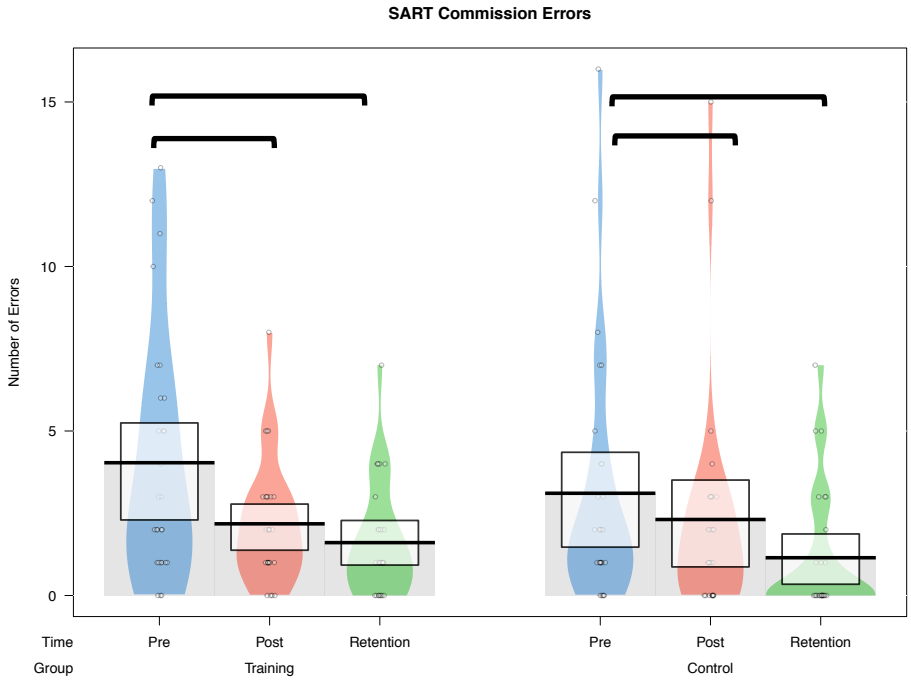

Figure 3.6-12 Pirate plot indicating numbers of commission errors made across sessions for the training and control groups. For the training group, the 95% HDI at the retention-test falls below the interval for the pre-test session, indicating a high probability that Error scores were reliably lower at retention. No other reliable differences across session or group can be observed.

3.6.8 Mental Rotation

The outcome variable for the mental rotation task was median Reaction Time.

Data Cleaning:

Trials that have reaction times <150ms were excluded from this analysis. Only trials for which correct answers were given were used in the analysis of reaction time data. The adjusted boxplot method was used to identify potential outliers, and 33 values were detected, 29 as falling below the lower extreme fence (1408ms), 19 training values originating from 4 participants (6 pre, 3 post, 10 retention) and 11 control values originating from 5 participants (3 pre, 2 post, 5 retention). Four values fell above the upper extreme fence (14,709ms); all control values (1 pre-test score, 2 post-test scores and 1 retention-test score). Outliers were removed prior to further analysis.

Model:

The MCMCglmm model included Time and Degree of Rotation (levels= 0°, 45°, 90°, 135°, 180°) as designated fixed effects, with Gender included as a covariate. Participants crossed with Time (levels = pre, post, retention) was included as a random effect Age was included in the model as a covariate (random effect), as was judged to be

the model of best fit by the (DIC). Planned contrasts analysed differences in median Reaction Time collapsed across degree of rotation. In order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's *f*) were calculated.

Data Analysis:

For the training group, the median RT values were, for all rotation angles and the overall median, shorter following training than prior to training. In contrast, for the control group, the median RT values were for all rotation angles longer following training than prior to training. Planned contrasts looking at pairwise comparisons across time for both groups found no medium to large differences in Median RT across Time for either the training or control group. Median RTs decreased for the training group, and increased for the control group, however no substantial (f > 0.25) differences were observed.

Table 3.6-11 Changes in Median RT Scores

	Pre	**Post**	**Retention**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
Group	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Training	4300 (298)	3393 (293)	3246 (297)	**0.000***	**0.23**	394	0.000*	0.13	394
Control	4279 (549)	4602 (550)	3985 (546)	0.310	0.05	394	0.359	0.02	394

* indicates p<0.05. Medium and large effect sizes (Cohen's *f* >0.25) in bold.

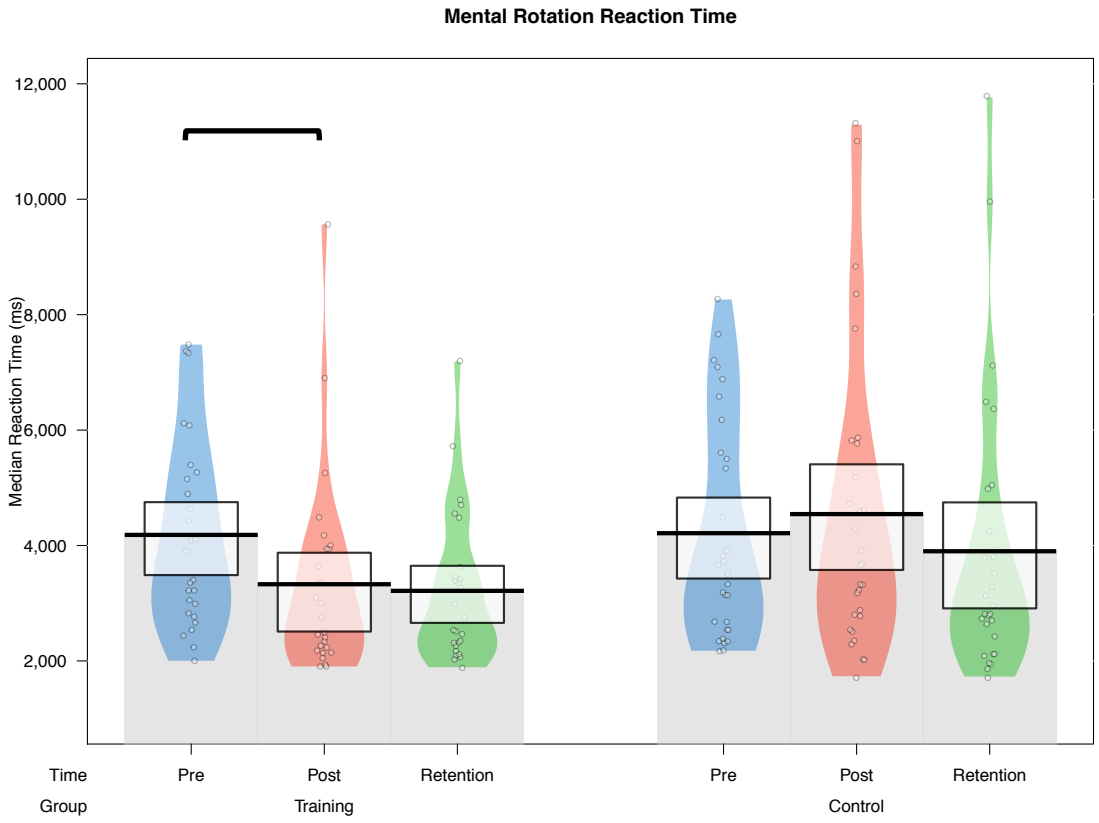

Figure 3.6-13 Pirate plots showing median Reaction Time scores for the training and control groups across sessions. In the training group, RT scores were lower at post and retention sessions. Analysis of the 95% confidence intervals indicate that the group means for the post- and retention-sessions fall below the reliable interval for the pre-test session. In contrast, the median RT score increases post-test in the control group, however no reliable differences across session can be observed.

3.6.9 Wisconsin Card Sorting Task

Results are split into 4 categories: Total number of errors, conceptual level responses, perseverative error, perseverative responses. Kongs, Thomson, Iverson, & Heaton, 2000, propose that total number of errors and conceptual level responses (CLRs) are working memory indices, whereas perseverative errors and perseverative responses measure cognitive flexibility.

Model:

For all outcome variables, the MCMCglmm model included Time as a designated fixed effect, with Gender included as a covariate. Participants crossed with Time (levels = pre, post, retention) were included as a random effect. Age was included in the model as a covariate (random effect), as was judged to be the model of best fit by the (DIC). In

order to assist in the interpretation of the inferential analyses, effect size indices (Cohen's ***f***) were calculated.

3.6.9.1 Total Number of Errors

'Total error' scores are the sum of all incorrect responses, i.e. the sum of perseverative, non-perseverative and unique errors (unique errors are errors where the stimulus card and the response card do not match on any dimension). Data were screened for outliers using the adjusted boxplots method, and no outliers were identified.

Analysis:

Planned contrasts using pairwise comparisons to examine the Total Errors across sessions revealed that in the training group, Total Error scores were lower at post-intervention than at the pre-test session (p=0.006, Cohen's f=0.36). Similarly, in the training group, scores at retention were lower than at pre-test (p<0.000, Cohen's f=0.25). Both contrasts were accompanied by medium effect sizes (Cohen's $f \geq 0.25$). For control group participants, no difference in Total Error performance was observed at post-intervention or at retention.

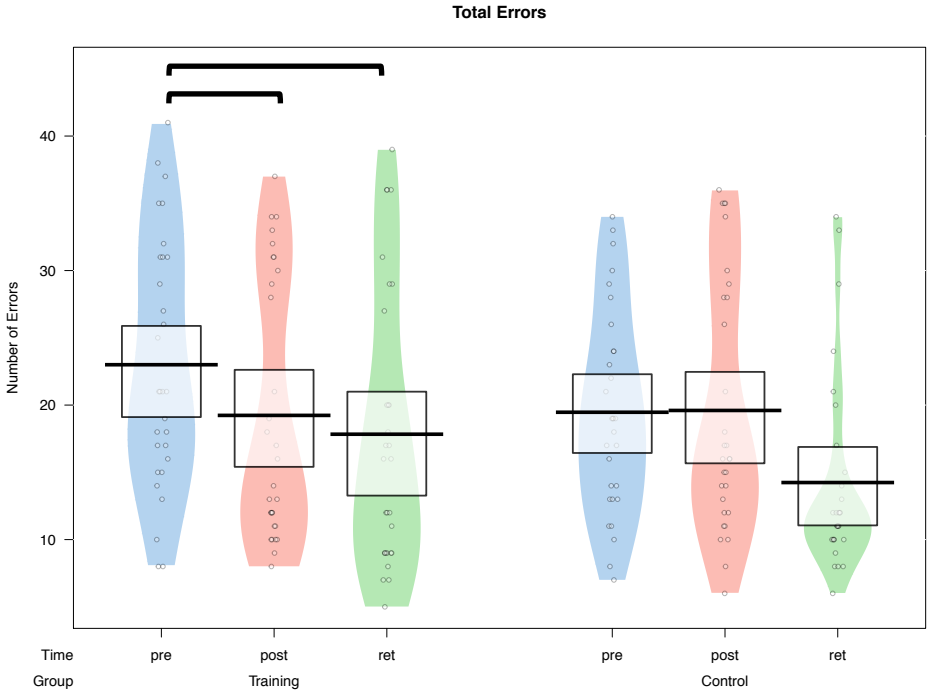

Figure 3.6-14 Pirate plot of total errors across session for Training and Control Groups. Total error scores decreased across session for the Training group participants. The majority of the 95% HDI in the retention group falls below the pre-test interval, indicating that it is reliable that the mean error score was lower at retention. For the controls, no reliable difference from the pre-test score is seen in perseverative error scores in the post-session, however at retention a reliable difference was observed, with lower retention total errors.

3.6.9.2 Conceptual Level Responses

Conceptual level responses (CLRs) are the number of correct responses that occur in runs of three or more – expressed as a percentage of the number of trials. Increase in conceptual level responses is indicative of improved performance on this task. No outliers were identified using the adjusted boxplots method.

Analysis:

Planned contrasts using pairwise comparisons to look at the CLRs across sessions found that in the training group, in comparison to pre-tests CLRs, scores were higher at post-intervention ($p=0.002$, Cohen's $f=0.41$) and at retention ($p<0.000$, Cohen's $f=0.29$). These were medium ($f>0.25$) to large ($f>0.4$). For control group participants, no difference in CLR performance was observed at post-intervention or at retention.

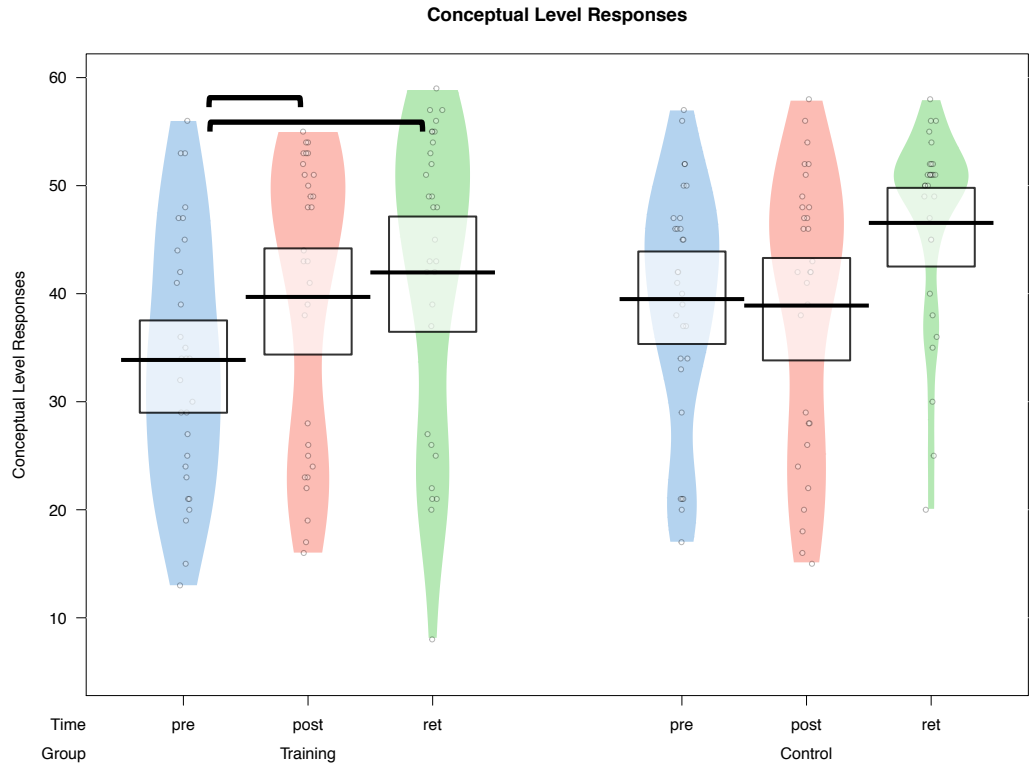

Figure 3.6-15 Pirate plot of Conceptual Level Responses (CLRs) across session for Training and Control Groups. Scores increased across session for the Training group participants. The mean post-test score for the training group falls above the pre-test mean. We can state with moderate confidence that the retention-test group mean for CLRs was higher than at pre-test, as the 95% HDIs barely overlap. For the controls, no difference is seen between pre- and post-test, however again retention-test group mean for CLRs was higher than at pre-test and the 95% HDI for the retention falls above that of the pre-session.

*3.6.9.3 **Perseverative Errors***

Perseverative Errors are errors occurring when the participant incorrectly uses the same rule for their choice as the previous choice. No outliers were identified using adjusted boxplots, and all data was included in the analysis.

Analysis:

Planned contrasts using pairwise comparisons across sessions revealed no systematic differences in the number of Perseverative Errors across session for the training or control groups.

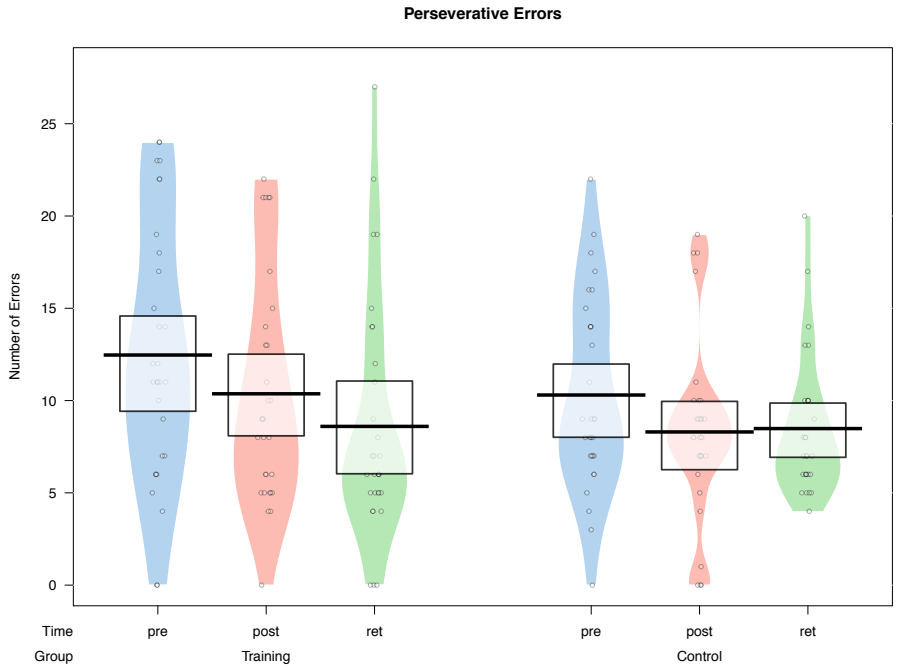

Figure 3.6-16 Pirate plot of perseverative errors across session for Training and Control Groups. Perseverative error scores decreased across session for the Training group participants. The majority of the 95% HDI in the retention group falls below the pre-test interval, indicating that it is reliable that the mean error score was lower at retention. For the controls, no reliable difference is seen in perseverative error scores across sessions.

*3.6.9.4 **Perseverative Responses***

Perseverative responses are the number of incorrect responses occurring when participants keep incorrectly applying the rule that would have been correct for the previous category.

Data Cleaning:

Outlier screening was carried out in an asymmetrical fashion for Perseverative error scores, as low-value scores (e.g. 1 or 0) are indicative of a high level of

performance, thus were retained. For perseverative responses, 6 values were identified as falling outside the upper extreme fence (30). These values all originated from the training group (3 pre-test, 1 post, 2 retention).

Analysis:

No reliable systematic changes in perseverative error scores were observed for either the control or training group across session.

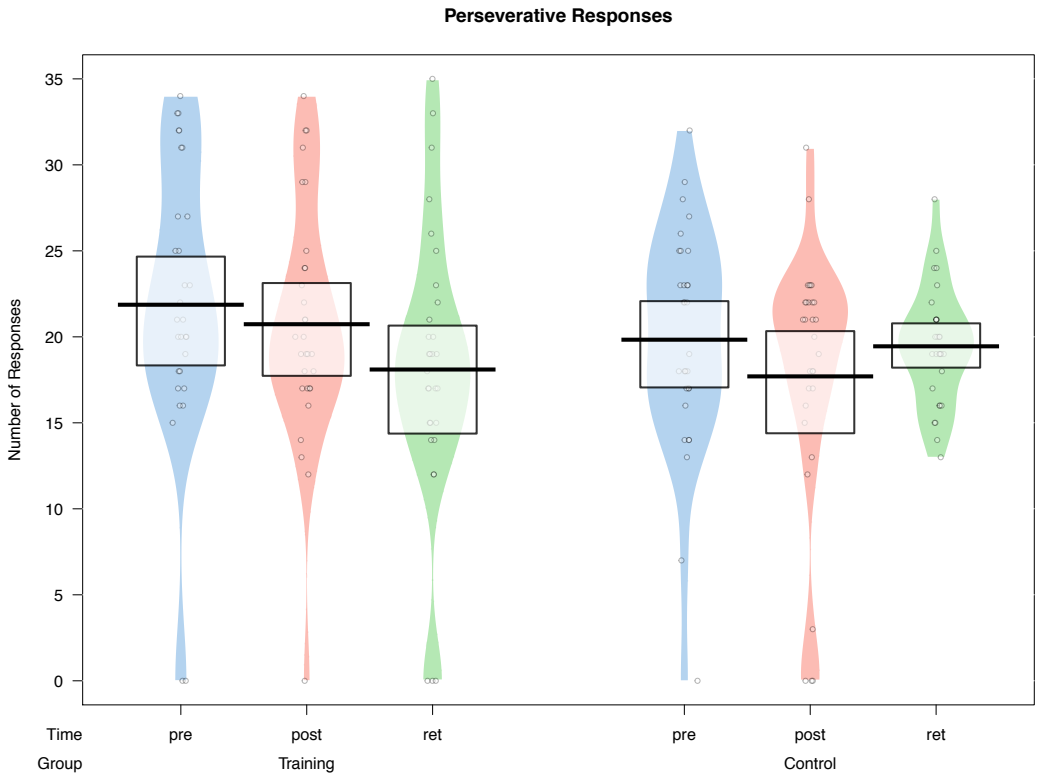

Figure 3.6-17 Pirate plot of perseverative responses across session for Training and Control Groups. Scores decreased across session for the Training group participants, however as the 95% HDIs are mostly overlapping, it cannot be said with certainty that the group means are different. For the controls, no reliable difference is seen across session.

Table 3.6-12 Wisconsin Card Sorting Task Means, Pre-Post and Pre-Retention Contrasts.

		Pre	**Post**	**Ret**	**Pre-Post contrasts**			**Pre-Retention contrasts**		
	Condition	***Mean (SE)***	***Mean (SE)***	***Mean (SE)***	***p***	***f***	***df***	***p***	***f***	***df***
Total Errors	Training	24.52 (2.64)	20.74 (2.63)	19.35 (2.63)	**0.006***	**0.36**	58	**0.000***	**0.25**	58
	Control	19.01 (1.64)	19.12 (1.65)	13.69 (1.65)	0.948	0.01	57	0.001*	0.22	57
Conceptual Level Responses	Training	32.12 (3.47)	37.94 (3.46)	40.21 (3.49)	**0.002***	**0.41**	58	**0.000***	**0.29**	58
	Control	40.06 (2.32)	39.46 (2.34)	47.22 (2.36)	0.796	0.03	57	0.002*	0.21	57
Perseverative Errors	Training	13.61 (1.72)	11.50 (1.72)	9.75 (1.72)	0.116	0.21	58	0.005*	0.19	58
	Control	10.01 (0.91)	8.02 (0.88)	8.21 (0.92)	0.079	0.23	58	0.123	0.11	58
Perseverative Responses	Training	20.88 (1.62)	20.66 (1.56)	17.35 (1.58)	0.906	0.02	55	0.061	0.13	55
	Control	19.54 (1.31)	17.41 (1.32)	19.19 (1.33)	0.170	0.18	58	0.815	0.02	58

3.6.10 Grip Strength and Dexterity

Grip Strength: No differences in grip strength were observed between the pre-test session and the post-test or retention-test session for either the motor training group or the active control group.

Dexterity: No differences in dexterity were observed between the pre-test session and the post-test or retention-test session for either the motor training group or the active control group.

3.6.11 Experiment 2: Tabular Summary of Compiled Results

Table 3.6-13 Experiment 2: Cognitive Results Summary Table

	Training							Control						
Cognitive Test	**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**		**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**	
Flanker	**Pre**	**Post**	**Retention**	**P**	***f***	**p**	***f***	**Pre**	**Post**	**Retention**	**p**	***f***	**p**	***f***
Conflict Cost	56.21(6.18)	52(6.02)	44.29(6.06)	0.459	0.10	0.038*	0.14	53.20(5.30)	53.08(5.34)	55.28(5.31)	0.978	0.00	0.649	0.03
CRT														
Cog RT	454(19.2)	458(19.5)	440(19.4)	0.666	0.05	0.133	0.09	475 (19)	469(19.2)	454(19.2)	0.560	0.06	0.063	0.11
Motor RT	360(33.5)	354(33.7)	325(34.1)	0.275	0.12	0.014*	0.14	349(30.6)	328(30.4)	315(30.7)	0.073	0.20	0.007*	0.15
n-Back Task Vis Accuracy														
1-back	.933 (.054)	.917 (.054)	.946 (.055	0.761	0.06	0.813	0.04	.965 (.051)	.966 (.051)	1.00 (.052)	0.984	0.01	0.410	0.15
2-back	.577 (.054)	.665 (.054)	.793 (.054)	0.092	0.22	**0.000***	**0.27**	.554 (.052)	.668 (.051)	.752 (.052)	**0.011***	**0.41**	**0.000***	**0.34**
Visual RT														
1-back	585 (70.9)	607 (70.3)	587 (71.4)	0.793	0.13	0.978	0.01	601 (80)	594 (81.3)	562 (82.6)	0.948	0.04	0.719	0.15
2-back	769 (72)	860 (71.2)	764 (70.3)	0.276	0.22	0.951	0.01	827 (83.2)	769 (79.7)	861 (84.4)	0.600	0.12	0.762	0.04

Table 3.6-13 Experiment 2: Cognitive Results Summary Table *(continued)*

	Training							Control						
Cognitive Test	**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**		**Mean (SE)**			**Pre-Post Contrast**		**Pre-Retention Contrast**	
Dual n-Back	**Pre**	**Post**	**Retention**	**P**	***f***	**p**	***f***	**Pre**	**Post**	**Retention**	**p**	***f***	**p**	***f***
Vis Accuracy														
1-back	.707 (.054)	.797 (.054)	.860 (.055)	0.086	0.28	0.003*	0.24	.791 (.05)	.848 (.051)	.828 (.051)	0.193	0.21	0.407	0.06
2-back	.209 (.057)	.352 (.055)	.267 (.056)	**0.012***	**0.32**	0.309	0.04	.302 (.054)	.311 (.053)	.366 (.053)	0.846	0.03	0.185	0.07
Aud Accuracy														
1-back	.864 (.045)	.902 (.045)	.911 (.045)	0.386	0.12	0.276	0.10	.887 (.042)	.938 (.042)	.947 (.043)	0.277	0.20	0.207	0.10
2-back	.448 (.045)	.494 (.045)	.574 (.045)	0.307	0.11	0.005*	0.15	.557 (.043)	.532 (.044)	.559 (.043)	0.608	0.07	0.951	0.00
Visual RT														
1-back	1366 (71.6)	1312 (71)	1254 (70.6)	0.510	0.09	0.171	0.09	1318 (80)	1207 (81.8)	1289 (80.4)	0.309	0.15	0.788	0.02
2-back	1462 (76.6)	1699 (72.7)	1540 (73.4)	**0.008***	**0.28**	0.378	0.04	1737 (86.8)	1738 (84)	1514 (85)	0.995	0.00	0.056	0.11
Auditory RT														
1-back	1267 (74.9)	1149 (75)	1080 (74.2)	0.180	0.20	0.032*	0.15	1165 (62.1)	1074 (62.1)	1088 (62.9)	0.236	0.19	0.322	0.08
2-back	1584 (76)	1467 (73.9)	1609 (74.9)	0.187	0.14	0.779	0.02	1560 (63.7)	1473 (65.3)	1564 (63.9)	0.279	0.11	0.954	0.00
TMT														
Ratio Score	1.336 (.038)	1.248(.039)	1.246 (.038)	0.030*	0.19	0.024*	0.10	1.308 (.049)	1.306 (.048)	1.312 (.048)	0.943	0.01	0.917	0.01

Table 3.6-13 Experiment 2: Cognitive Results Summary Table *(continued)*

SART														
Errors														
Omission	6.36 (1.45)	3.88 (1.45)	2.94 (1.46)	**0.012***	**0.34**	0.001*	0.24	8.07 (1.93)	5.37 (1.90)	3.96 (1.94)	**0.048***	**0.27**	0.003*	0.20
Commission	4.03 (0.57)	2.18 (0.56)	1.61 (0.57)	**0.002***	**0.44**	**0.000***	**0.28**	3.47 (0.73)	2.34 (0.74)	1.55 (0.75)	**0.021***	**0.31**	**0.000***	**0.26**
Rotation Task														
Reaction Time	4300 (298)	3393 (293)	3246 (297)	0.000*	0.23	0.000*	0.13	4279 (549)	4602 (550)	3985 (546)	0.310	0.05	0.359	0.02
WCST														
Total Errors	24.5 (2.64)	20.7 (2.63)	19.4 (2.63)	**0.006***	**0.36**	**0.000***	**0.25**	19.0 (1.64)	19.1 (1.65)	13.7 (1.65)	0.948	0.01	0.001*	0.22
CLRs	32.1 (3.47)	37.9 (3.46)	40.2 (3.49)	**0.002***	**0.41**	**0.000***	**0.29**	40.1 (2.32)	39.5 (2.34)	47.2 (2.36)	0.796	0.03	0.002*	0.21
Persev Errors	13.6 (1.72)	11.5 (1.72)	9.8 (1.72)	0.116	0.21	0.005*	0.19	10.0 (0.91)	8.0 (0.88)	8.2 (0.92)	0.079	0.23	0.123	0.11
Persev Resp	20.9 (1.62)	20.7 (1.56)	17.4 (1.58)	0.906	0.02	0.061	0.13	19.5 (1.31)	17.4 (1.32)	19.2 (1.33)	0.170	0.18	0.815	0.02

3.7 Kinematic Data

3.7.1 Summary

Adaptation to the Baseline Motor Task

At the post-test session, changes were seen in performance on the baseline motor task for training group only for three kinematic measures:

1. **Lower Path Deviation:** the training group exhibiting lower Path Deviation for the trained limb at the retention session, whereas this effect was not seen in controls.
2. **Decreased Peak Velocity:** Peak Velocity was lower following motor training at both post-test and retention-test for the trained limb.
3. **Peak Velocity reached later in movement trajectory:** Time at Peak Velocity was later following motor training at both post-test and retention-test for the trained limb.

No reliable changes were seen for the training group on measures of heading error, movement time or spectral arc length. For the control group, no reliable changes were seen on the baseline motor task for any movement characteristics at the post-intervention or retention test sessions.

Association between adaptation to the motor task, and performance in cognitive measures

To establish whether there were relationships between the measures of adaptation derived for the individual participants to the baseline motor task, and the degree of improvement exhibited by those individuals on the tests of cognitive function, statistical measures of were calculated for assessments of cognitive function for which reliable changes from pre- to post-intervention had been obtained.

For the Motor Training group, there was an association between the VM adaptation measure manifested by individual participants, and the pre- to post-training percentage improvement in the WCST conceptual level responses. No such reliable associations were present for any of the other improved cognitive outcome measures following training. In addition, no relationship was seen between cognitive outcome measures and adaptation to the VM for individuals in the control group.

3.7.2 Data Processing and Analysis

See Experiment 1 kinematic data and analysis section for an outline of the data processing and analyses steps (Section 2.6.2). Identical steps were taken in the analysis of the kinematic characteristics in experiment 2. Additionally, a brief analysis of the change in the percentage of targets acquired on the visuomotor training task between Day 1, Block 1 and Day 5, Block 5 is included (Section 1.1.21-1.1.22).

Model:

For all movement characteristics, the MCMCglmm model included Time (levels = pre, post, retention) crossed with Limb (levels= Left, Right), Block (levels= 1, 2, 3, 4), and Target (levels = flexion, flexion-radial, radial, extension-radial, extension, extension-ulnar, ulnar, flexion-ulnar) was a designated fixed effect. Participants crossed with Limb, Time and Target were included as random effects.

Planned Contrasts:

For each of the movement characteristics outlined above, least square means obtained prior to the intervention (pre), following the intervention (post) and at a retention session following a period of no training (ret) were compared, and planned contrasts were carried out on the mean differences using pairwise comparisons. Separate analyses were carried out for the intervention (Motor Training) and active control (Control) groups.

All contrasts were carried out between the fourth block of the baseline task on day one, and the first block of the baseline task at the subsequent post-test and retention-test sessions. This was in effort to avoid inadvertently biasing the pre-test scores, as early adaptation to the task would occur rapidly over the initial blocks of the task at the pre-test session. In order to 'wash-out' these effects and exclude them from analysis, only the fourth block of the baseline task was included.

In addition to examining the left (trained) limb, the performance of the right, untrained limb was also considered. The objective was to assess the generality of the adaptations that arose from the five days of training. To effects of this nature – when expressed as changes in the performance of the untrained limb, the terms "cross education" and "interlimb transfer" have been applied.

3.7.3 Movement Time

Movement time (MT) was calculated as the period that elapsed from movement onset to target acquisition.

3.7.3.1 Motor Training Group

Left (training) limb: Movement Time scores were higher following training than prior to training in the case of two targets, 'extension-radial' and 'extension-ulnar', indicating that following training participants took longer to respond to these targets. These effects were not present at retention. Movement Time was not different to pre-test for any other targets across post-test or retention test sessions.

Right (transfer) limb: Movement Time scores were not reliably and systematically different from pre-test scores at either the post-test or retention test sessions for the right limb.

3.7.3.2 Control Group:

For participants carrying out the control intervention, Movement Time scores were not reliably and systematically different from pre-test scores at either the post-test or retention test sessions with one exception: right-hand movements to the 'flexion' target had a lower MT at retention ($p=0.025$) than at pre-test.

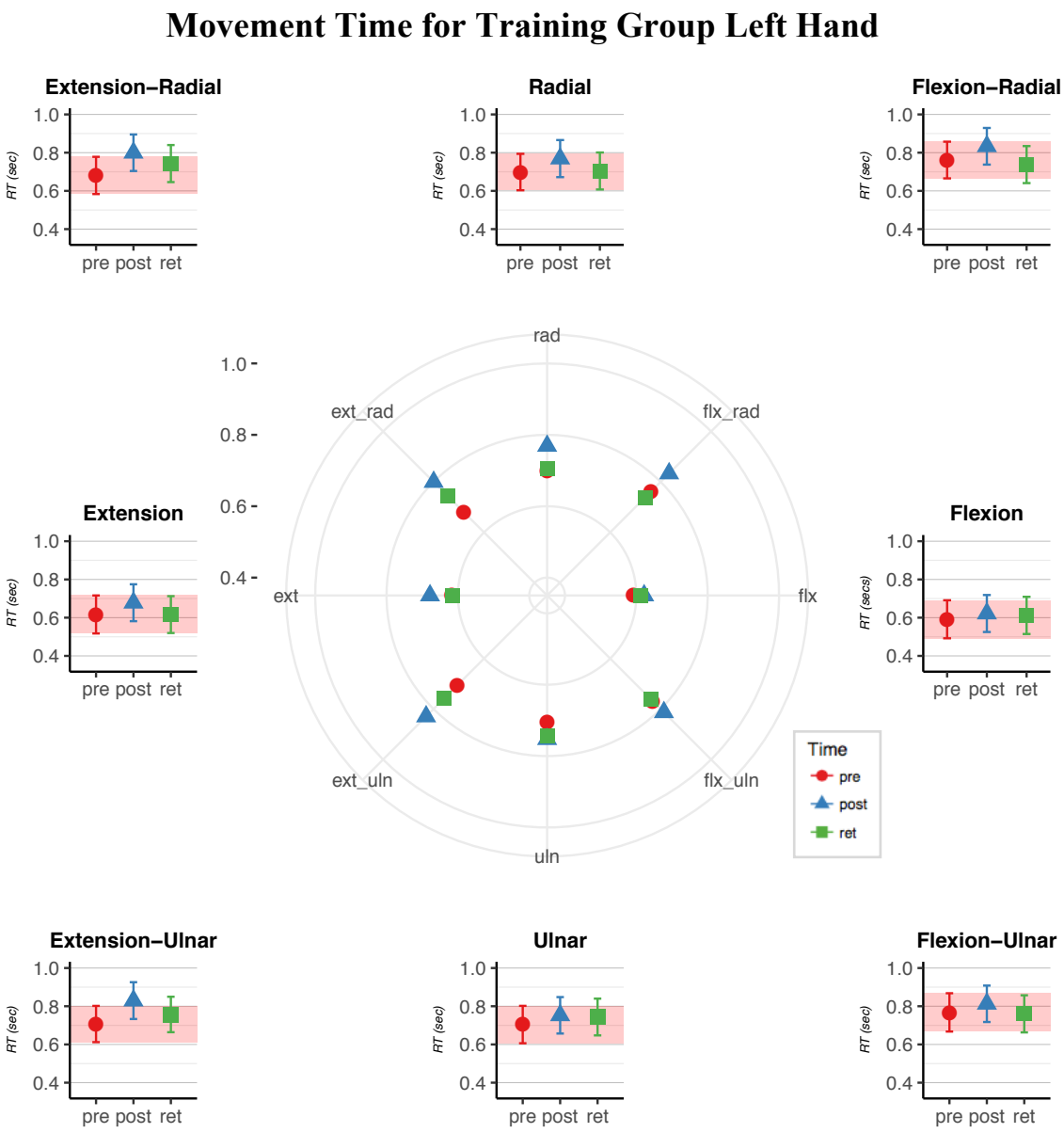

Figure 3.7-1 Changes in LH Movement Time for the Training Group across all anatomical targets. For the 'extension-radial' and 'extension-ulnar' targets, post-test scores are lower than at the pre-test session. Across all targets, an increase in MT is observed from pre-test to post-test, however by the retention session, the MT values appear similar to, or shorter than, those recorded prior to the intervention.

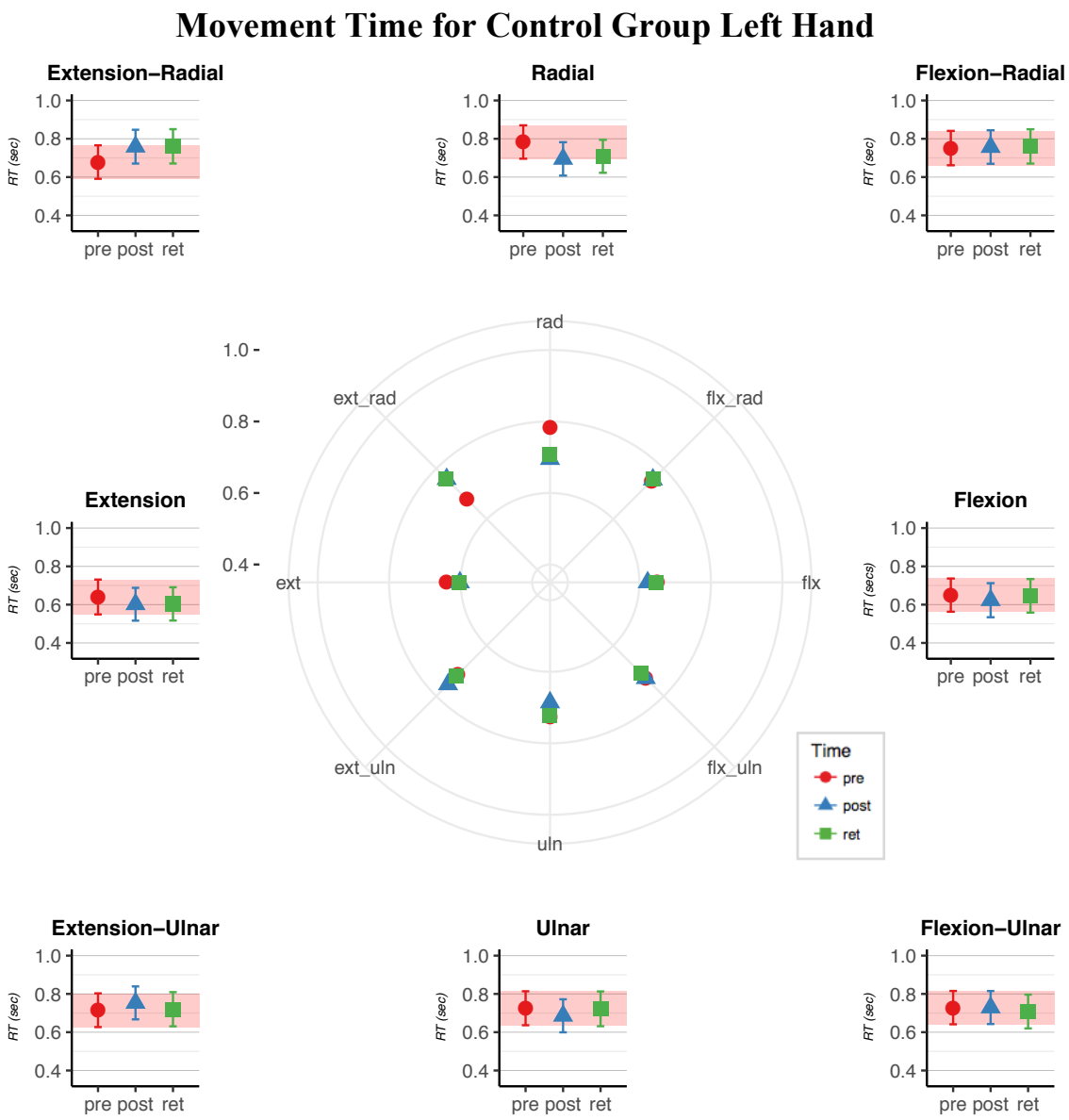

Figure 3.7-2 Changes in LH Movement Time for the Control Group across all anatomical targets. MT post-test and retention-test scores cannot reliably be distinguished from pre-test scores across target locations, with all post-test and retention-test means all fall within the 95% confidence intervals for the pre-test score.

Table 3.7-1 Pre-Post and Pre-Retention contrasts for Movement Time: Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.592	0.622	0.612	0.538	0.682	0.650	0.623	0.646	0.572	0.938
	flx_rad	0.761	0.833	0.738	0.126	0.615	0.751	0.757	0.760	0.906	0.857
	rad	0.699	0.769	0.704	0.142	0.912	0.783	0.695	0.708	0.059	0.112
	ext_rad	0.681	0.800	0.743	**0.017***	0.205	0.678	0.759	0.760	0.089	0.081
	ext	0.617	0.678	0.616	0.212	0.990	0.640	0.602	0.604	0.425	0.441
	ext_uln	0.707	0.830	0.757	**0.013***	0.276	0.715	0.753	0.720	0.414	0.913
	uln	0.704	0.753	0.744	0.327	0.414	0.725	0.686	0.722	0.391	0.950
	flx_uln	0.768	0.813	0.760	0.354	0.874	0.728	0.729	0.708	0.990	0.669

Table 3.7-1 Pre-Post and Pre-Retention contrasts for Movement Time: Training and Control Groups (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.634	0.689	0.656	0.246	0.641	0.698	0.663	0.592	0.464	**0.025***
	flx_rad	0.737	0.750	0.721	0.774	0.732	0.667	0.733	0.666	0.158	0.983
	rad	0.703	0.698	0.665	0.913	0.437	0.713	0.697	0.672	0.731	0.383
	ext_rad	0.636	0.670	0.679	0.463	0.361	0.674	0.682	0.640	0.867	0.472
	ext	0.671	0.632	0.652	0.417	0.697	0.657	0.664	0.624	0.891	0.487
	ext_uln	0.745	0.777	0.751	0.510	0.900	0.698	0.732	0.705	0.469	0.892
	uln	0.658	0.698	0.692	0.391	0.475	0.713	0.710	0.664	0.947	0.291
	flx_uln	0.711	0.724	0.680	0.771	0.524	0.694	0.714	0.631	0.685	0.183

3.7.4 Intervention Group Movement Time: Visuomotor Training Task

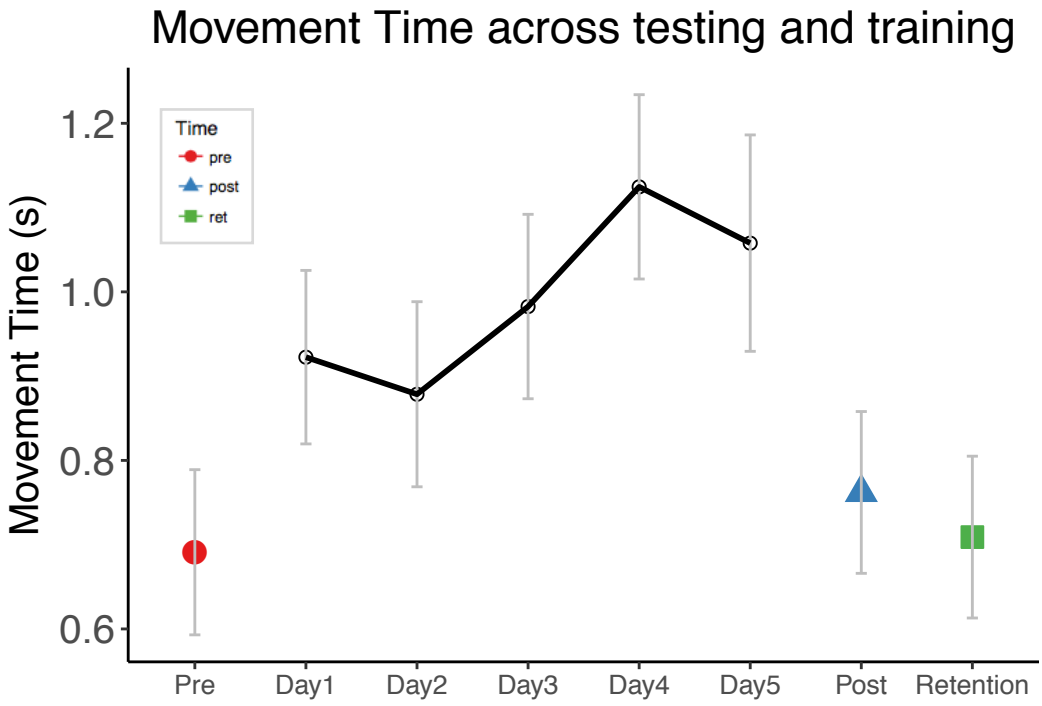

Figure 3.7-3 Changes in 3.7.3 Intervention Group Movement Time across Testing Sessions and Training Days. The average MT across all targets is shown for each testing session, Pre, post and retention. In addition, the average MT across training day is shown, connected with a blue line. Mean movement time on the visuomotor training task increases from training Day 1 to training Day 5. MT is greater at the post-test following training than at pre-test.

A significant increase in Movement Time from Day 1 to Day 5 ($p= 0.032$) was observed as task difficulty increased.

Table 3.7-2: Mean Training Movement Time values by Training Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	0.923 (0.053)	0.820, 1.025	-
Day 2	0.878 (0.056)	0.769, 0.988	0.424
Day 3	0.983 (0.056)	0.873, 1.092	0.258
Day 4	1.125 (0.056)	1.015, 1.234	**0.000***
Day 5	1.058 (0.066)	0.929, 1.186	**0.031***

* indicates $p<0.05$

3.7.5 Spectral Arc Length: Baseline Visuomotor Task

Pre-acquisition Spectral Arc Length (SAL) is the smoothness of the movement trajectory for the interval between movement onset and initial contact with the Target zone (the area within 10% of the target radius). SAL values that are further from zero indicate 'less smooth' movement trajectories.

3.7.5.1 Motor Training Group

Left (training) limb: For one target, 'flexion-radial', SAL was significantly lower (more negative) following the training intervention, at both post-test ($p= 0.012$) and retention sessions ($p=0.028$). No other reliable differences in SAL were seen across targets for the left limb, across post-test and retention-test sessions.

Right (transfer) limb: No interlimb transfer was observed for measures of SAL, with post-test and retention-test scores showing no systematic differences in comparison to the pre-test session.

3.7.5.2 Control Group:

In comparison to the pre-test, neither left nor right limb session contrasts found any systematic differences in SAL measures across all targets for the control group.

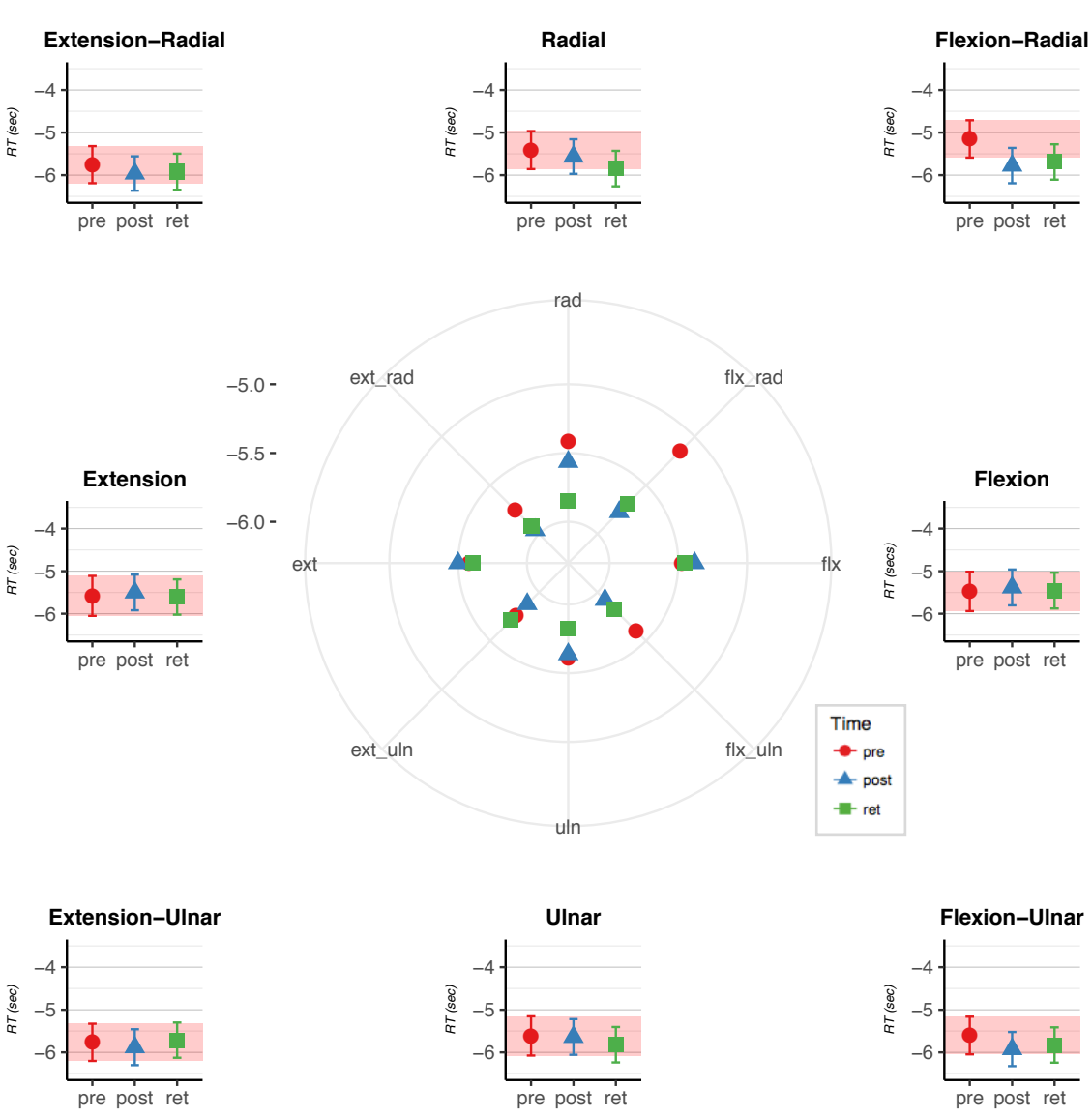

Figure 3.7-4 Training Group differences in SAL for the left hand across Sessions. Compared to the pre-test, SAL was lower (more negative) at post-test and the retention session for the flexion-radial target, indicating that the movement was less smooth. All other measures of SAL were not reliably different following training at either the post-test or retention-test sessions in comparison to pre-test measures.

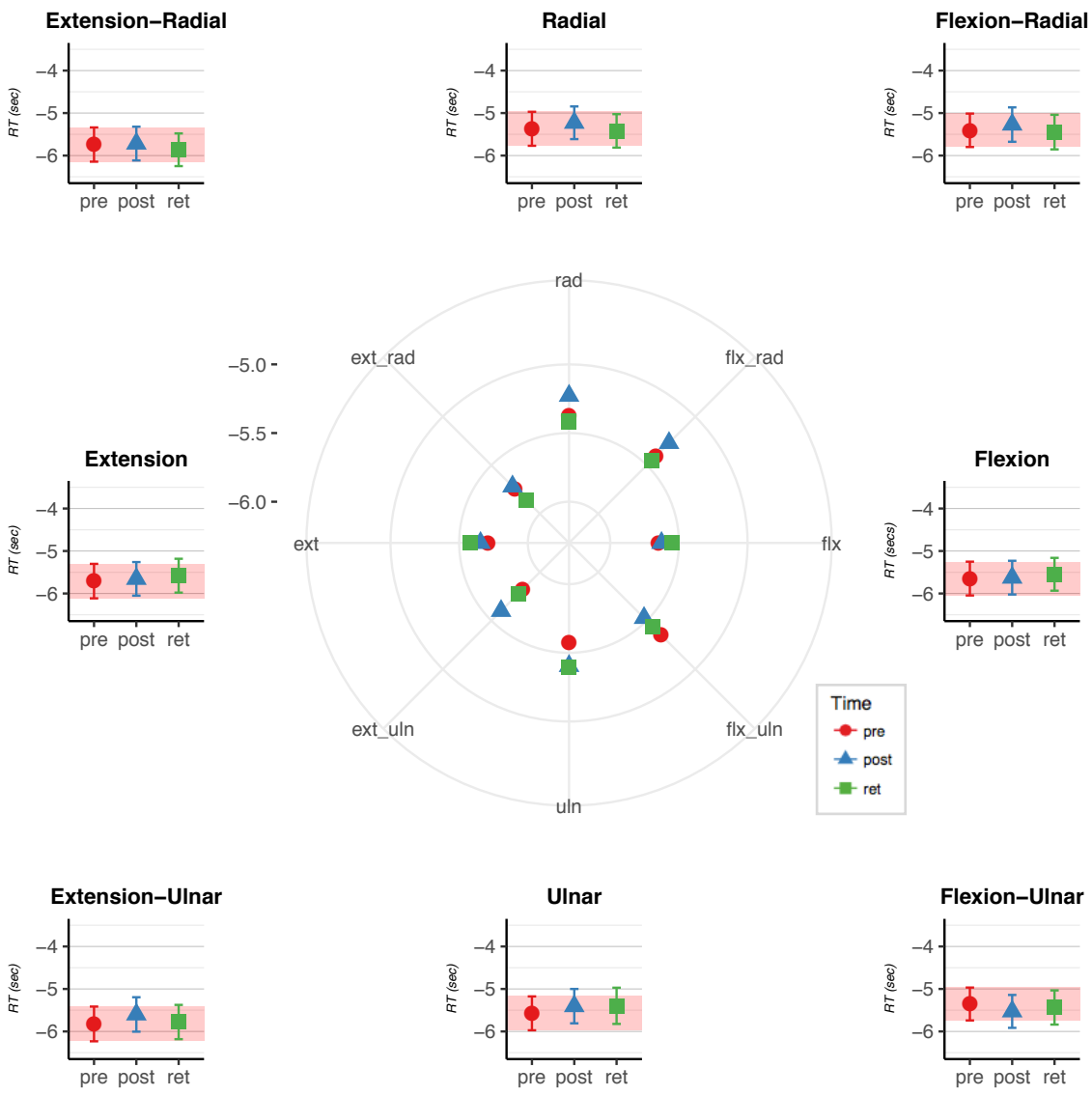

Figure 3.7-5 Control Group differences in SAL for the left hand across Sessions. Measures of SAL were not reliably different following training at the pre-test or retention-test sessions in comparison to pre-test measures.

Table 3.7-3 Pre-post and Pre-Retention contrasts for pre-Acquisition SAL: Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	-5.475	-5.381	-5.456	0.709	0.939	-5.649	-5.627	-5.548	0.929	0.676
	flx_rad	-5.149	-5.775	-5.691	**0.012***	**0.028***	-5.406	-5.271	-5.448	0.582	0.862
	rad	-5.411	-5.564	-5.846	0.524	0.077	-5.370	-5.229	-5.419	0.553	0.835
	ext_rad	-5.754	-5.961	-5.920	0.389	0.498	-5.741	-5.718	-5.864	0.923	0.611
	ext	-5.580	-5.500	-5.607	0.751	0.913	-5.708	-5.655	-5.581	0.830	0.609
	ext_uln	-5.764	-5.879	-5.713	0.635	0.827	-5.823	-5.600	-5.778	0.367	0.855
	uln	-5.614	-5.638	-5.821	0.922	0.420	-5.574	-5.404	-5.397	0.476	0.459
	flx_uln	-5.604	-5.923	-5.827	0.198	0.363	-5.354	-5.528	-5.436	0.451	0.727

Table 3.7-3 Pre-postand Pre-Retention contrasts for pre-Acquisition SAL: Training and Control Groups (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	-5.599	-5.923	-5.449	0.182	0.532	-5.588	-6.067	-5.718	0.057	0.605
	flx_rad	-5.321	-5.469	-5.359	0.551	0.868	-5.165	-5.608	-5.465	0.074	0.233
	rad	-5.472	-5.789	-5.906	0.176	0.069	-5.773	-5.527	-5.325	0.327	0.077
	ext_rad	-5.517	-5.869	-5.775	0.147	0.280	-5.610	-5.934	-5.662	0.177	0.832
	ext	-5.547	-5.553	-5.540	0.980	0.978	-5.934	-6.004	-5.928	0.773	0.980
	ext_uln	-5.773	-6.025	-5.990	0.307	0.360	-5.872	-5.852	-5.794	0.931	0.750
	uln	-5.800	-5.893	-5.867	0.697	0.780	-5.586	-5.512	-5.614	0.758	0.910
	flx_uln	-5.551	-5.691	-5.903	0.560	0.136	-5.656	-5.712	-5.451	0.826	0.429

3.7.6 Intervention Group Spectral Arc Length: Visuomotor Training

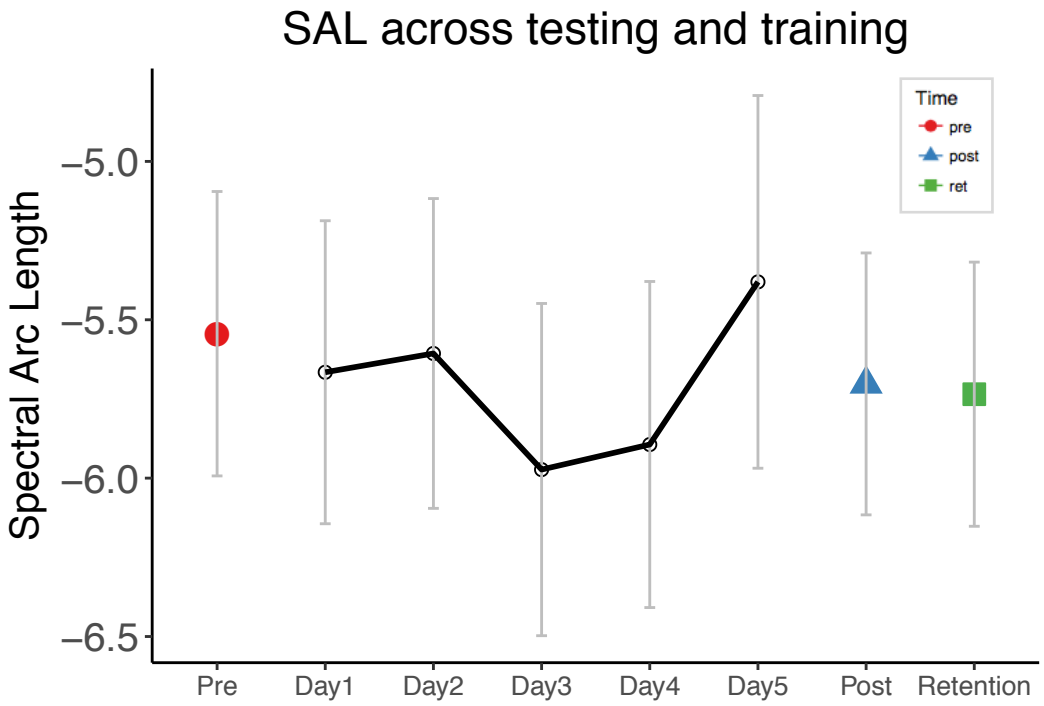

Figure 3.7-6 Changes in intervention group Spectral Arc Length across Testing Sessions and Training Days. The average SAL across all targets is shown for each testing session, Pre, post and retention. In addition, the average SAL across training day is shown in the centre of the figure, connected with a blue line. Mean SAL on the visuomotor training task appears to move in an upward trend from training Day 1 to training Day 5. SAL is slightly more negative at the post-test following training than at pre-test, indicating lower mean smoothness.

No significant change in Spectral Arc Length was observed from Day 1 to Day 5 of training (p= 0.329), despite increasing task difficulty.

Table 3.7-4: Mean Training Spectral Arc Length values by Training Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	-5.666 (0.244)	-6.144, -5.187	-
Day 2	-5.606 (0.250)	-6.095, -5.117	0.819
Day 3	-5.973 (0.268)	-6.497, -5.449	0.249
Day 4	-5.894 (0.263)	-6.409, -5.379	0.395
Day 5	-5.380 (0.300)	-5.969, -4.792	0.329

3.7.7 Path Deviation: Baseline Visuomotor Task

Pre-Acquisition Path Deviation (PD) is a measure of the spatial characteristics of movement trajectory between movement onset and initial contact with the Target zone (the area within 10% of the target radius). PD indicates the overall magnitude of deviance from the straight-line trajectory between movement onset position and target.

3.7.7.1 Motor Training Group

Left (training) limb: For the training limb, PD was lower for the 'flexion-radial' target post-intervention ($p=0.001$), and this effect was also seen at retention ($p=0.052$). No other differences were seen at the post-test. However, for the retention session, PD was lower for four additional targets: 'radial' ($p=0.000$), 'extension-radial' ($p=0.030$), 'extension' ($p=0.002$), 'flexion-ulnar' ($p=0.024$)

Right (transfer) limb: Only two targets showed lower PD in comparison to pre-test values for the right limb: for the 'extension' target at post-test ($p=0.014$), and for the 'flexion-radial' target at the retention session ($p=0.002$). No other reliable differences were seen across targets.

3.7.7.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for the left limb. For the right limb, PD for the 'flexion' target was lower at both post-test ($p=0.003$) and retention-test ($p=0.004$). No other reliable differences were observed between pre-test PD values and post-test or retention session PD values for the right limb.

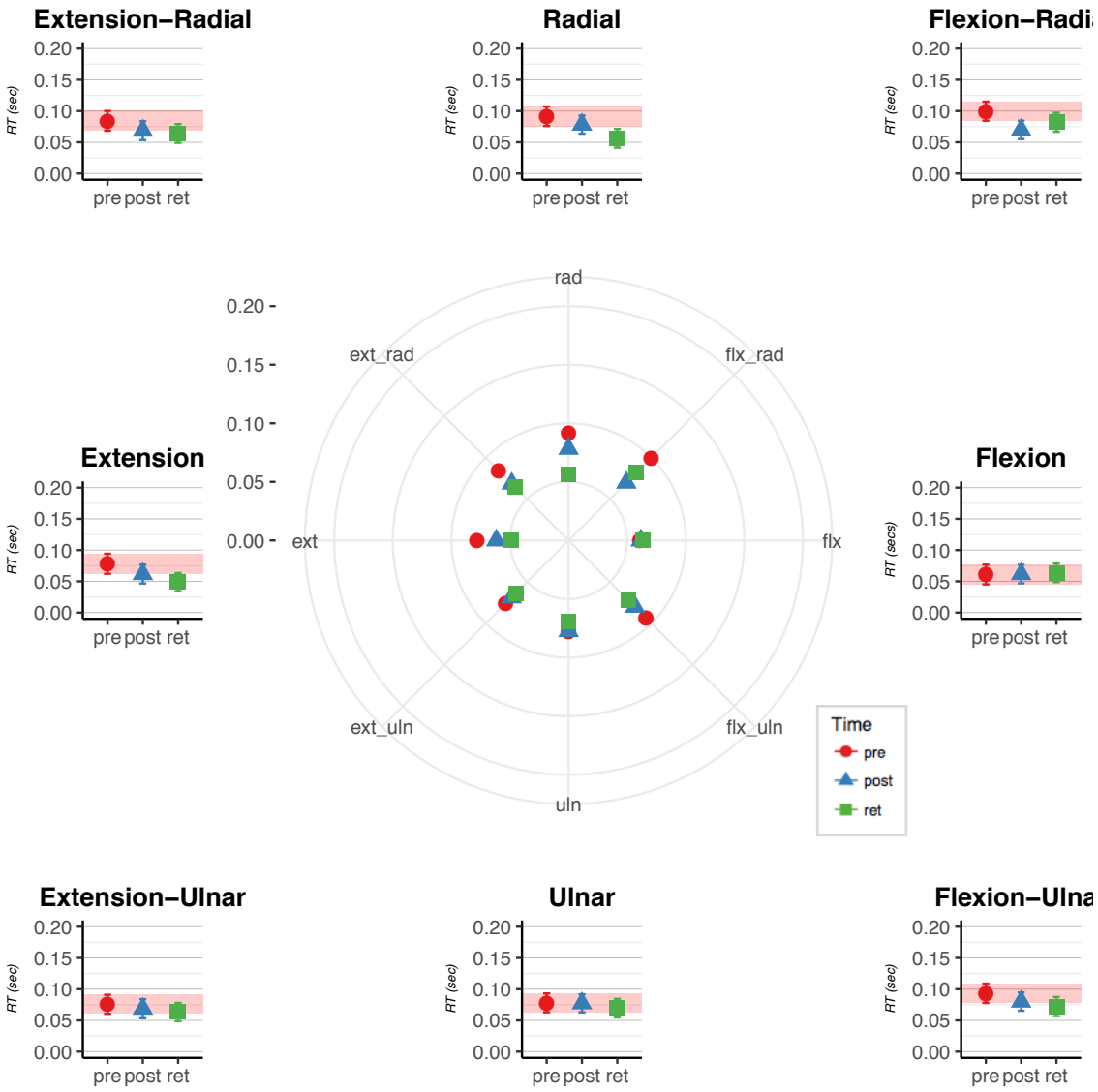

Figure 3.7-7 Changes in left-hand Path Deviation for all targets across sessions for the Training Group. For the targets at flexion-radial target, at both post-test and retention. Lower PD score was seen at the retention-test for the radial, extension-radial, extension and flexion-ulnar targets.

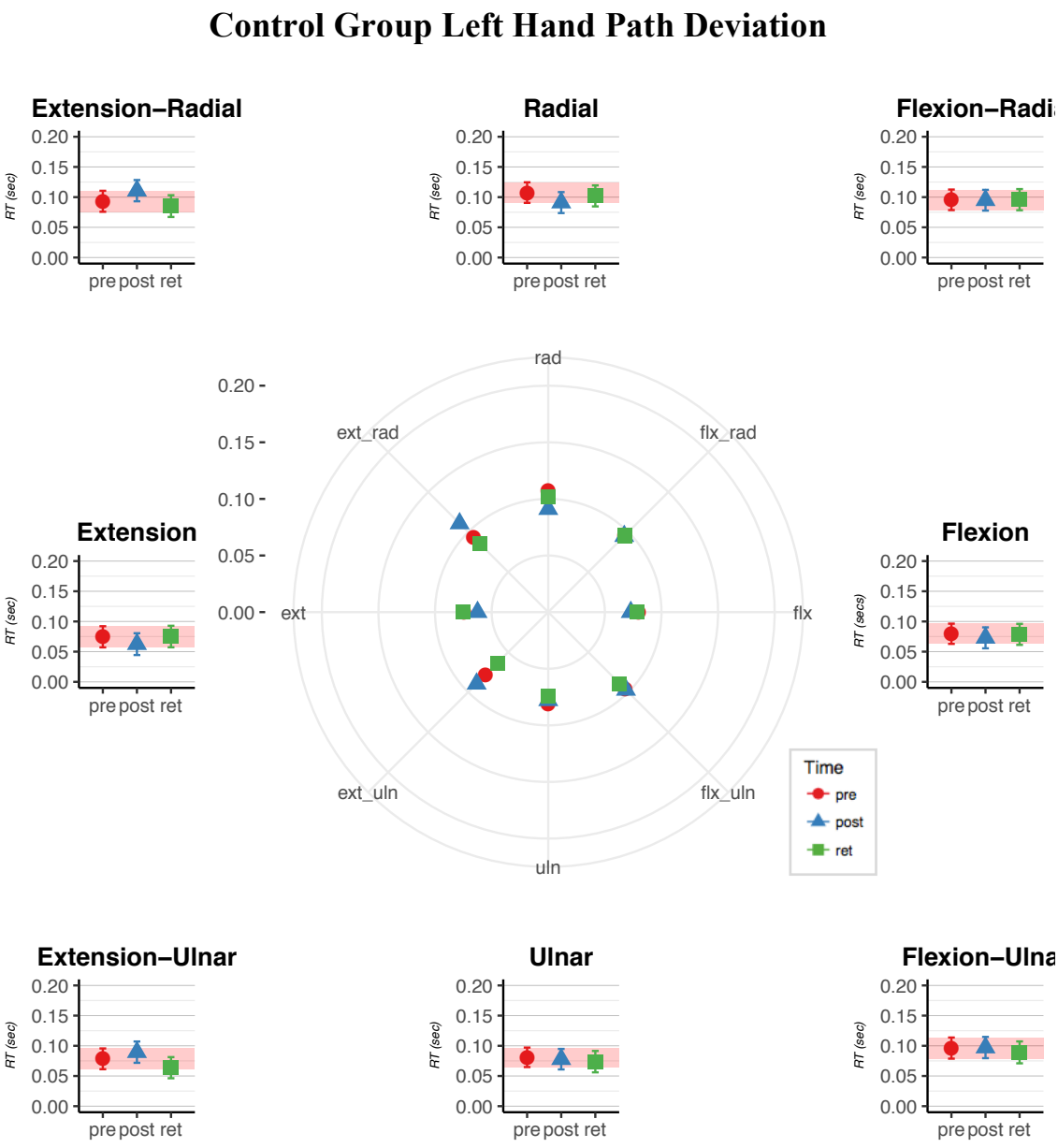

Figure 3.7-8 Changes in left-hand Path Deviation for the Control Group. No reliable differences in Path Deviation can be seen across sessions for any target location, with all post-test and retention-test means falling within the pre-test 95% confidence intervals.

Table 3.7-5 Pre–post and pre-retention contrasts for Path Deviation for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.061	0.062	0.064	0.933	0.764	0.080	0.073	0.079	0.521	0.927
	flx_rad	0.100	0.070	0.082	**0.001***	**0.052***	0.096	0.095	0.096	0.952	0.978
	rad	0.092	0.078	0.056	0.137	**0.000***	0.108	0.091	0.102	0.107	0.586
	ext_rad	0.084	0.069	0.064	0.091	**0.030***	0.093	0.111	0.085	0.091	0.450
	ext	0.078	0.062	0.049	0.086	**0.002***	0.075	0.062	0.075	0.263	0.968
	ext_uln	0.076	0.069	0.063	0.440	0.175	0.078	0.089	0.064	0.296	0.165
	uln	0.078	0.077	0.070	0.936	0.359	0.081	0.078	0.074	0.752	0.482
	flx_uln	0.093	0.080	0.072	0.145	**0.024***	0.096	0.097	0.089	0.931	0.510

Table 3.7-5 Pre–post and pre-retention contrasts for Path Deviation for the Training and Control Groups (continued)

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.074	0.061	0.065	0.172	0.289	0.103	0.071	0.073	**0.003***	**0.004***
	flx_rad	0.096	0.082	0.081	0.107	0.103	0.090	0.091	0.084	0.875	0.592
	rad	0.091	0.078	0.064	0.125	**0.002***	0.109	0.101	0.096	0.450	0.244
	ext_rad	0.074	0.064	0.068	0.242	0.500	0.089	0.076	0.076	0.191	0.187
	ext	0.072	0.050	0.058	**0.014***	0.091	0.060	0.066	0.061	0.578	0.916
	ext_uln	0.081	0.066	0.066	0.088	0.085	0.077	0.090	0.088	0.241	0.330
	uln	0.080	0.068	0.065	0.206	0.121	0.088	0.108	0.098	0.058	0.328
	flx_uln	0.083	0.074	0.071	0.281	0.138	0.110	0.109	0.078	0.913	0.002

3.7.8 Intervention Group Path Deviation: Motor Training

Mean Path deviation did not change reliably over the course of training Day 1 to Training Day 5, despite the increase in task difficulty.

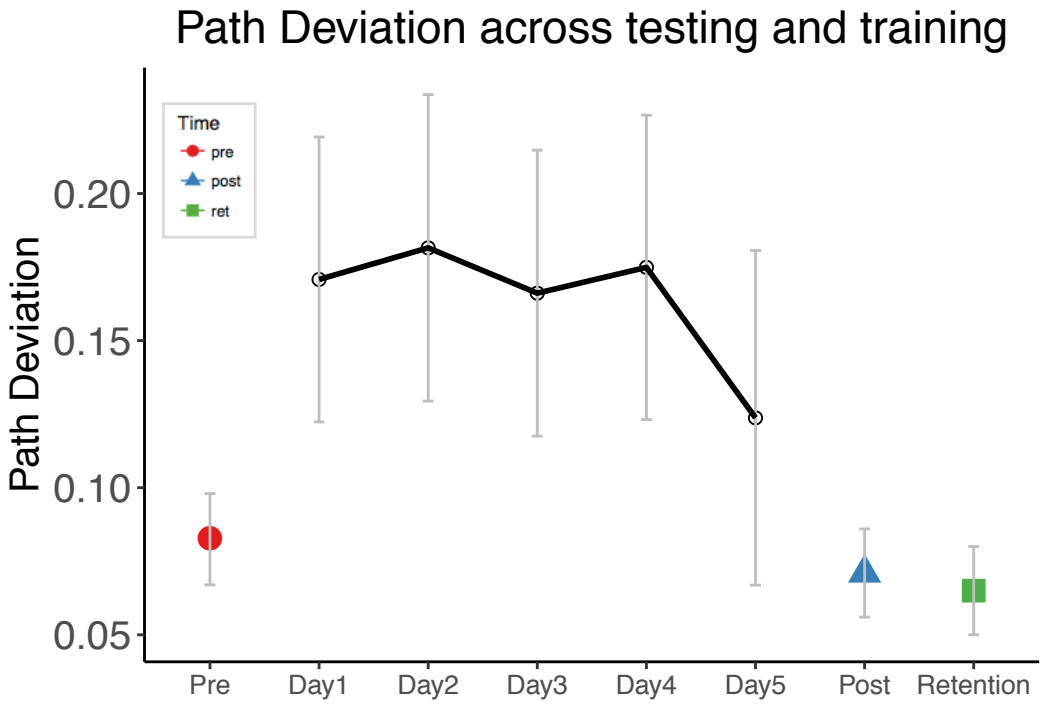

Figure 3.7-9 Changes in intervention group Path Deviation across Testing Sessions and Training Days. The average PD across all targets is shown for each testing session, Pre, post and retention. In addition, the average PD across training day is shown in the centre of the figure, connected with a blue line. Mean PD on the visuomotor training task appears to move in a downward trend from training Day 1 to training Day 5. PD is slightly lower at the post-test following training than at pre-test, indicating less path deviation in the movement trajectory, and at retention it is lower than at pre-test.

Table 3.7-6 Mean Training Pre Acquisition Path Deviation values by Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	0.171 (0.025)	0.122, 0.219	-
Day 2	0.182 (0.027)	0.129, 0.234	0.643
Day 3	0.166 (0.025)	0.118, 0.215	0.831
Day 4	0.175 (0.026)	0.123, 0.227	0.862
Day 5	0.124 (0.029)	0.067, 0.181	0.065

3.7.9 Peak Velocity

Peak Velocity (PV) is the maximum value of the rate of change of velocity for the interval between movement onset and target acquisition.

3.7.9.1 Motor Training Group

Left (training) limb: PV was lower at post-test in comparison to the pre-test for all target locations ($p<0.05$). This effect was seen at retention for all targets with the exception of the 'ulnar' target ($p=0.063$).

Right (transfer) limb: At the post-training session, PV was systematically lower for two out of the eight targets. These were the 'radial' ($p=0.019$) and 'extension-ulnar' targets ($p=0.027$). The other six post-test target values were not reliably Changes in left- different from PV values at pre-test. At the retention test, the 'radial' target remained lower than at pre-test ($p=0.010$), and in addition the 'ulnar' target was also lower at retention.

3.7.9.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for either the Left or Right limb. Similarly, no reliable differences were observed between pre-test PV values and retention session PV values.

Study 1: Training Group Left Hand Peak Velocity

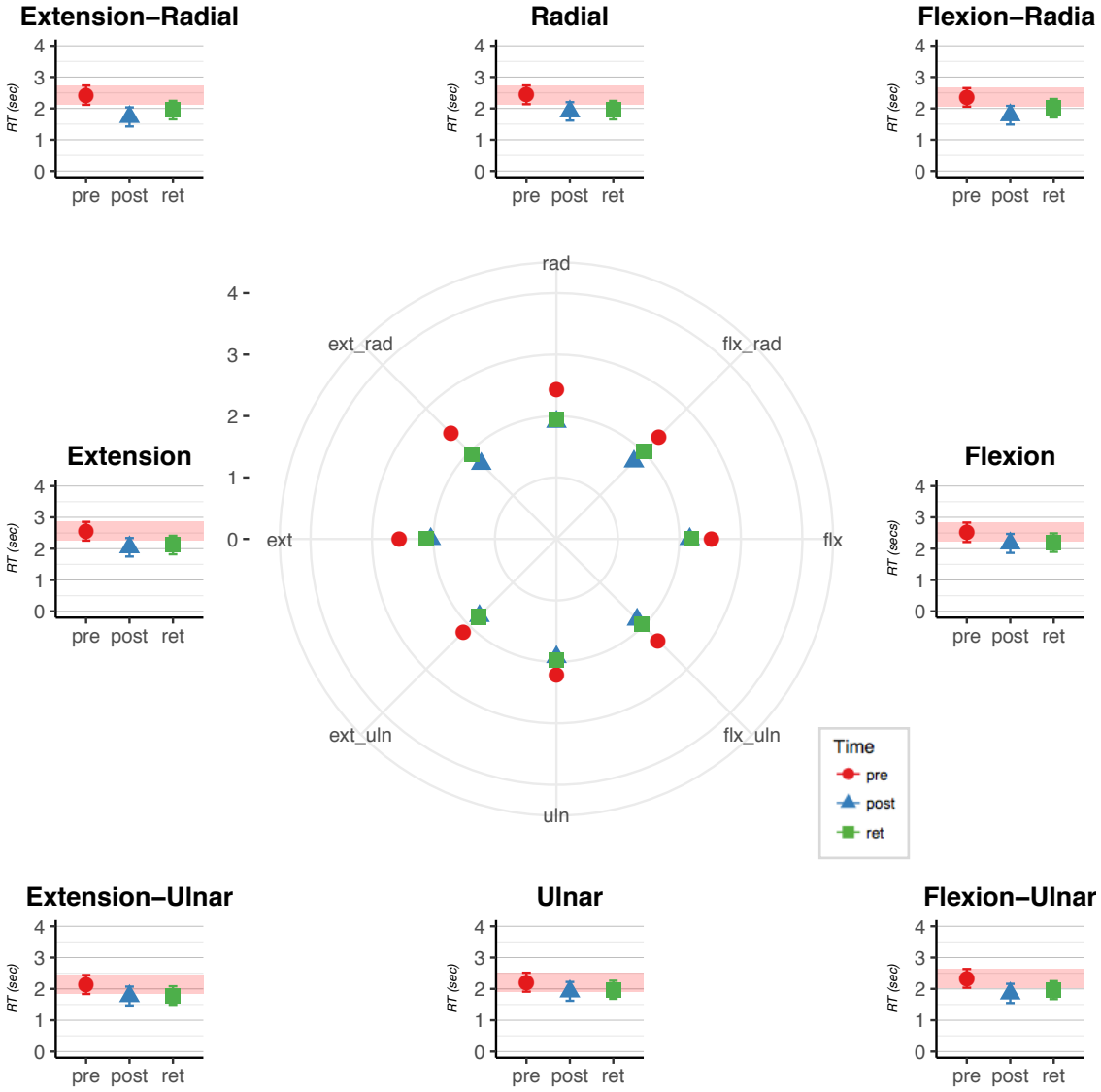

Figure 3.7-10 Changes in left-hand Peak Velocity for the training group across testing sessions. Systematic differences in Peak Velocity can be observed between pre-test and post-test sessions, and in all but one case (ulnar target), PV values remained lower at retention session in comparison to pre-test values.

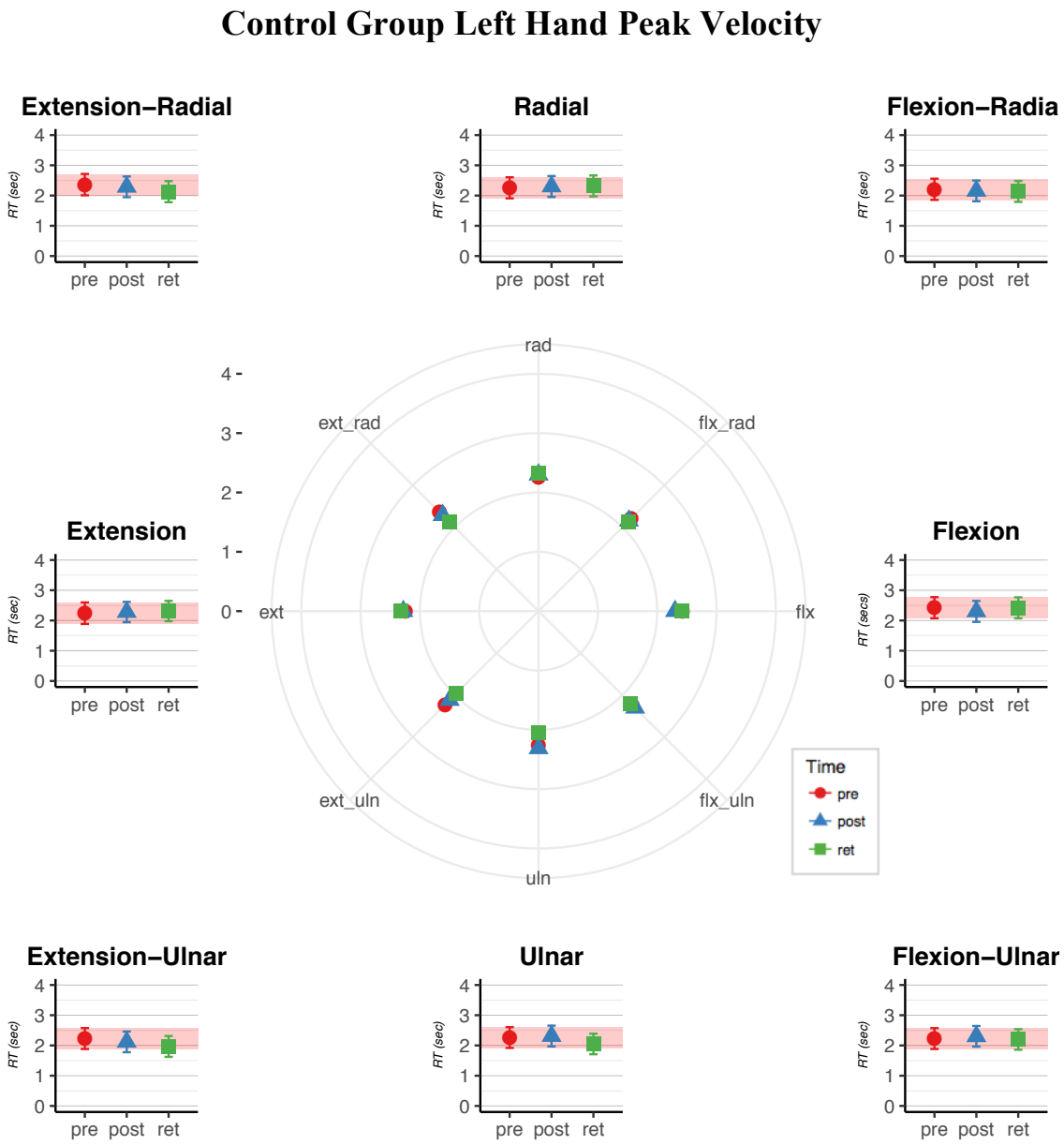

Figure 3.7-11 Changes in left-hand Peak Velocity for the control group across testing sessions. No systematic differences in Peak Velocity can be observed across sessions for any of the eight target locations.

Table 3.7-7 Pre–post and pre-retention contrasts in Peak Velocity for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	2.522	2.167	2.193	**0.007***	**0.018***	2.424	2.301	2.422	0.432	0.989
	flx_rad	2.354	1.783	2.007	**0.007***	**0.009***	2.207	2.155	2.137	0.741	0.658
	rad	2.434	1.906	1.945	**0.007***	**0.000***	2.256	2.299	2.319	0.788	0.689
	ext_rad	2.424	1.729	1.947	**0.007***	**0.000***	2.362	2.288	2.130	0.643	0.162
	ext	2.555	2.045	2.116	**0.007***	**0.002***	2.242	2.280	2.314	0.811	0.645
	ext_uln	2.140	1.771	1.787	**0.006***	**0.008***	2.229	2.118	1.967	0.499	0.095
	uln	2.213	1.920	1.971	**0.030***	0.063	2.262	2.312	2.049	0.751	0.181
	flx_uln	2.335	1.854	1.960	**0.000***	**0.005***	2.228	2.302	2.199	0.643	0.852

Table 3.7-7 Pre–post and pre-retention contrasts in Peak Velocity for the Training and Control Groups *(continued)*

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	2.324	2.067	2.178	**0.054**	0.291	2.449	2.315	2.539	0.413	0.566
	flx_rad	2.176	1.975	2.081	0.130	0.465	2.420	2.258	2.252	0.309	0.274
	rad	2.443	2.129	2.102	**0.019***	**0.010***	2.567	2.395	2.502	0.290	0.674
	ext_rad	2.261	2.039	2.011	0.102	0.062	2.503	2.209	2.196	0.079	0.051
	ext	2.181	2.078	2.171	0.447	0.942	2.269	2.135	2.147	0.411	0.443
	ext_uln	2.170	1.872	1.935	**0.027***	0.086	2.225	2.331	2.294	0.521	0.667
	uln	2.393	2.175	2.103	0.105	**0.034***	2.489	2.728	2.508	0.142	0.904
	flx_uln	2.277	2.071	2.242	0.125	0.793	2.535	2.612	2.444	0.622	0.563

3.7.10 Intervention Group Peak Velocity: Visuomotor Training Task

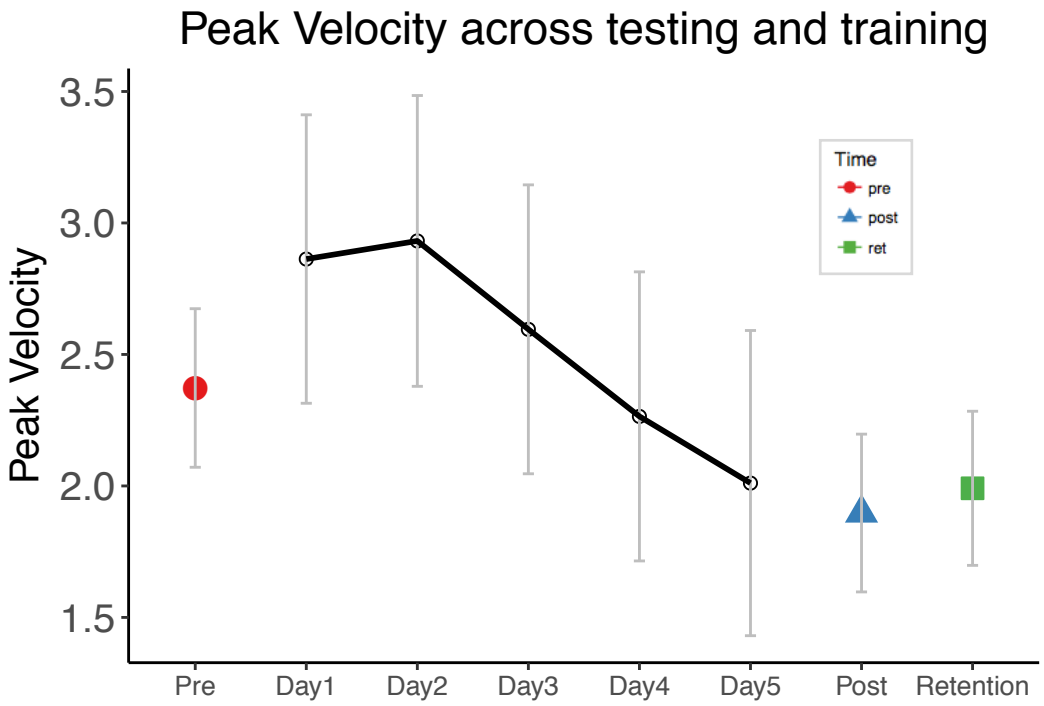

Figure 3.7-12 Changes in intervention group Peak Velocity across Testing Sessions and Training Days. The average PV across all targets is shown for each testing session, Pre, post and retention. In addition, the average PV across training day is shown in the centre of the figure, connected with a blue line. Mean PV on the visuomotor training task appears to move in a downward trend from training Day 1 to training Day 5. PV is lower at the post-test following training than at pre-test, indicating a lower peak velocity in the movement trajectory. At the retention session it is also lower than at pre-test.

A significant decrease in Peak Velocity was observed from Day 1 to Day 5 of the training task ($p = 0.002$).

Table 3.7-8 Mean Training Peak Velocity values by Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	2.863 (0.280)	2.314, 3.411	-
Day 2	2.932 (0.282)	2.379, 3.485	0.781
Day 3	2.596 (0.280)	2.046, 3.145	0.289
Day 4	2.264 (0.280)	1.715, 2.814	**0.020***
Day 5	2.011 (0.296)	1.431, 2.591	**0.002***

* indicates $p<0.05$

3.7.11 Peak Velocity Time

Peak Velocity time (PVT) is the time at which maximum velocity was reached during the interval between movement onset and target acquisition, or if participants failed to acquire the target, the interval between movement onset and timeout.

3.7.11.1 Motor Training Group

Left (training) limb: With the exception of the 'radial' target, PVT was longer at the post-test session across all other targets ($p<0.05$) than at the pre-test session, indicating that peak velocity was reached at a later stage in the movement trajectory. At the retention session, PVT values remained higher for the 'extension-radial' ($p=0.002$), 'extension' ($p=0.004$) and 'flexion-ulnar' ($p=0.002$) targets. No reliable differences were seen at retention for the other five targets in comparison to the pre-test.

Right (transfer) limb: At the post-training session, PVT was systematically longer for the right limb for four out of the eight targets. These were the 'extension' ($p=0.031$), 'extension-ulnar' ($p=0.001$), 'extension-ulnar' ($p<0.001$) and 'flexion-ulnar' targets (0.040). The remaining four post-test target values were not reliably Changes in left-different from PV values at pre-test. At the retention test, PVTs remained higher than at the pre-test for the 'extension' ($p=0.027$), 'extension-ulnar' ($p=0.002$) and 'flexion-ulnar' ($p=0.021$) targets. In addition, PVT values were higher for the 'radial' ($p=0.021$) and 'ulnar' ($p=0.050$) targets.

3.7.11.2 Control Group:

For the control group, only one systematic difference was observed across all targets at post-intervention for the left limb: at retention, PVT was later than at the pre-test ($p=0.006$). For the right limb, PVT was later at post-test for one target at the post-test session ($p=0.010$). No other reliable differences were observed between pre-test PVTs and retention session PVTs for either limb for the control group.

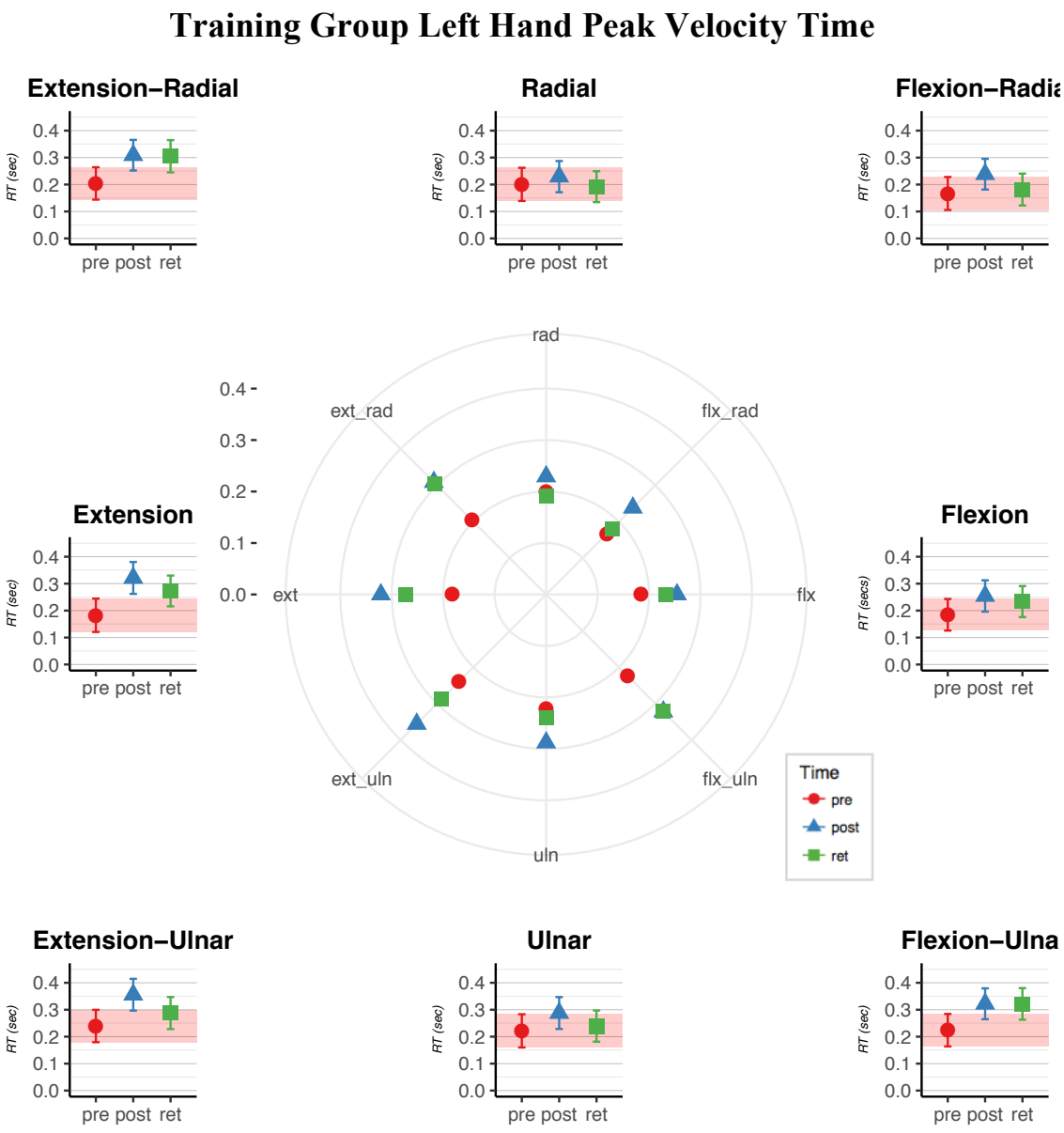

Figure 3.7-13 Changes in LH Peak Velocity Time for the Training Group across Sessions. With the exception of the radial target, higher PVT scores were observed across all targets at the post-test sessions in comparison to the pre-tests, indicating later time at peak velocity after the intervention. This difference remained at retention for the extension-radial, extension and flexion-ulnar targets. No other systematic changes in time at Peak Velocity were observed at retention.

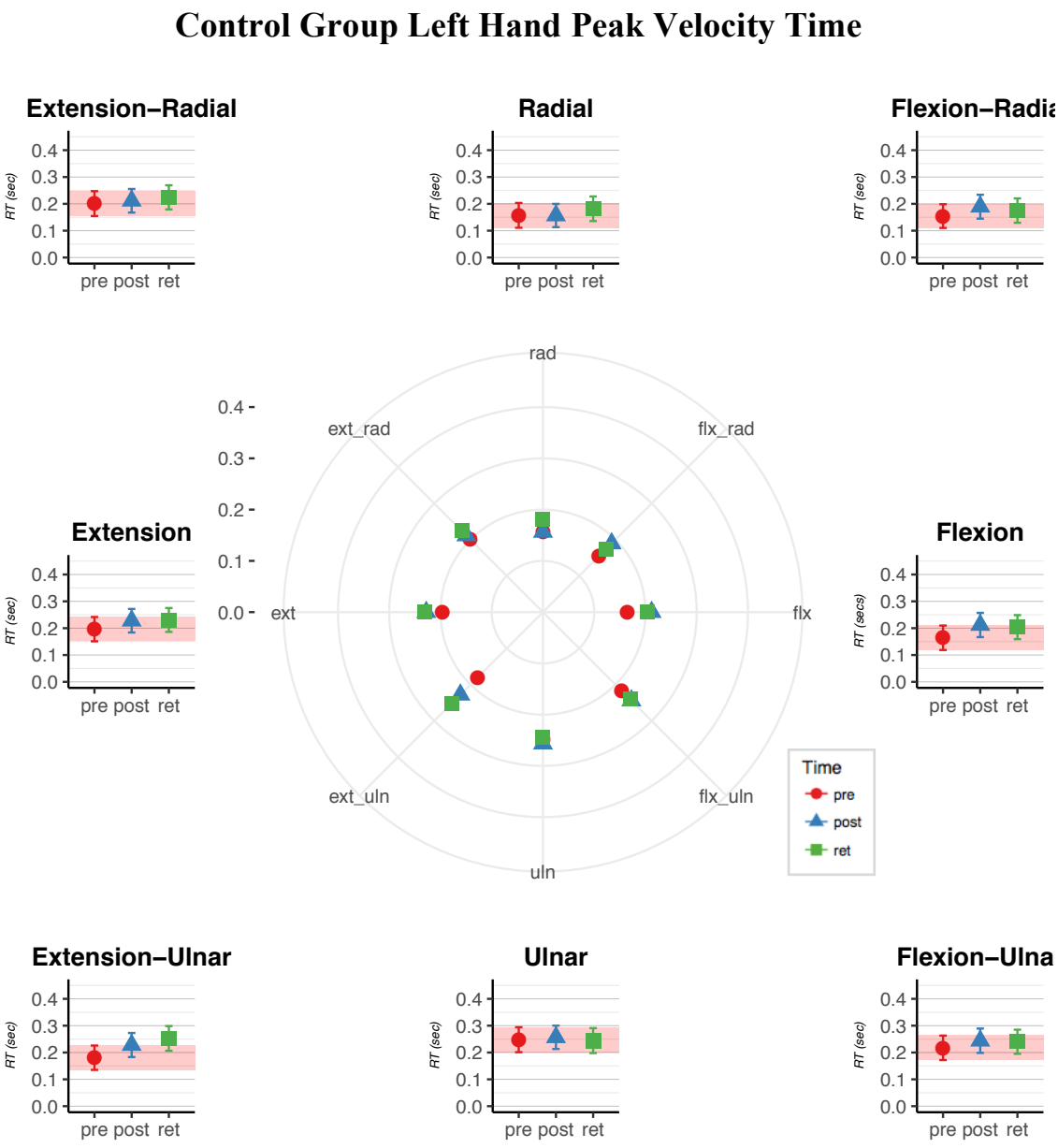

Figure 3.7-14 Changes in left-hand Time at Peak Velocity for the control group across testing sessions. No systematic differences in PVT can be observed at post-test sessions for any of the eight target locations. At retention, one difference is seen for the extension-ulnar target, with retention PVT higher than pre-test PVT.

3.7-9 Pre-post and pre-retention contrasts of Peak Velocity Time for the training and control groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	0.184	0.254	0.233	**0.026***	0.108	0.164	0.212	0.204	0.074	0.130
	flx_rad	0.167	0.238	0.181	**0.020***	0.647	0.154	0.189	0.175	0.186	0.431
	rad	0.200	0.229	0.192	0.362	0.788	0.157	0.156	0.182	0.980	0.352
	ext_rad	0.204	0.309	0.305	**0.001***	**0.002***	0.201	0.211	0.224	0.692	0.401
	ext	0.183	0.321	0.273	**0.000***	**0.004***	0.196	0.228	0.231	0.235	0.202
	ext_uln	0.240	0.356	0.288	**0.000***	0.127	0.181	0.228	0.252	0.066	**0.006***
	uln	0.222	0.288	0.239	**0.039***	0.586	0.248	0.257	0.244	0.735	0.907
	flx_uln	0.224	0.322	0.321	**0.002***	**0.002***	0.217	0.244	0.240	0.295	0.397

Table 3.7-9 Pre-post and pre-retention contrasts of Peak Velocity Time for the training and control groups (*continued)*

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	0.195	0.241	0.225	0.146	0.331	0.173	0.227	0.177	0.052	0.878
	flx_rad	0.198	0.220	0.236	0.510	0.221	0.155	0.183	0.176	0.291	0.426
	rad	0.177	0.221	0.250	0.153	**0.021***	0.135	0.152	0.167	0.542	0.242
	ext_rad	0.210	0.280	0.265	**0.031***	0.075	0.171	0.195	0.192	0.358	0.438
	ext	0.209	0.309	0.276	**0.001***	**0.027***	0.195	0.212	0.201	0.517	0.810
	ext_uln	0.210	0.334	0.301	**0.000***	**0.002***	0.171	0.244	0.208	**0.010***	0.176
	uln	0.199	0.232	0.261	0.297	**0.050***	0.161	0.211	0.183	0.067	0.412
	flx_uln	0.218	0.282	0.290	**0.040***	**0.021***	0.150	0.197	0.191	0.102	0.129

3.7.12 Intervention Group Peak Velocity Time: Visuomotor Training Task

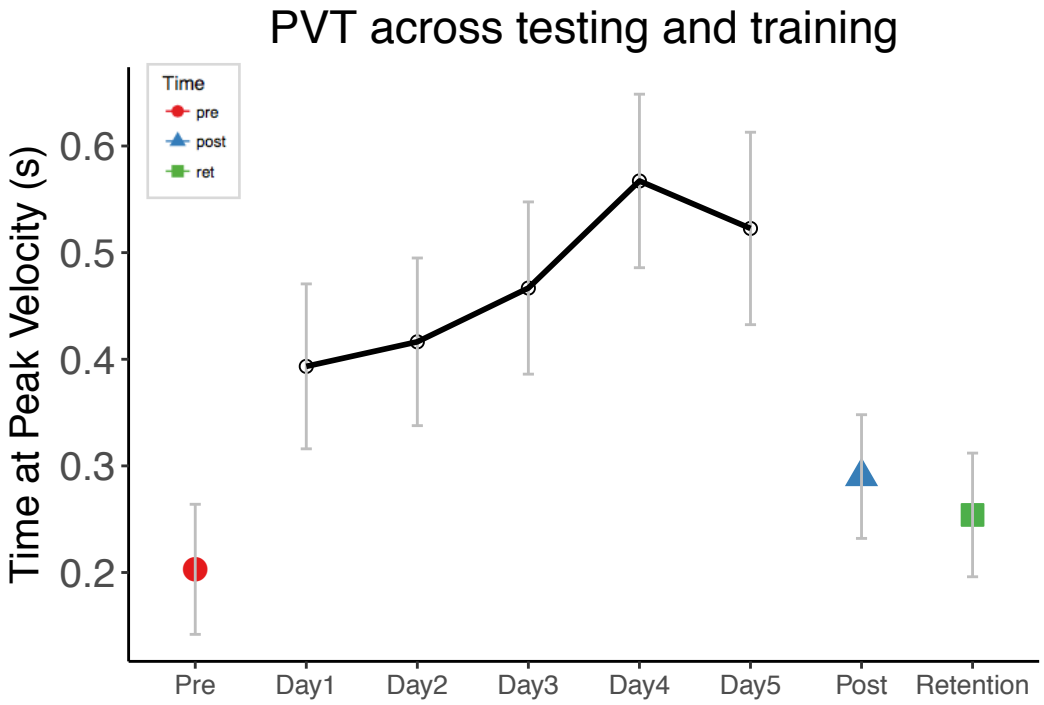

Figure 3.7-15 Changes in intervention group Time at Peak Velocity across Testing Sessions and Training Days. The average PVT across all targets is shown for each testing session: pre, post and retention. In addition, the average PVT across training day is shown in the centre of the figure, connected with a blue line. Mean PVT on the visuomotor training task appears to increase from training Day 1 to training Day 5. PVT is higher at the post-test following training than at pre-test, indicating a later peak velocity in the movement trajectory. At the retention session, it is also later than at pre-test.

An increase in Peak Velocity Time was observed from training Day 1 to training Day 5 on the visuomotor training task (p= 0.002). Mean PVT values increased over the course of training, indicating a later time in the movement trajectory at which PV was reached. After the intervention, performance on the baseline visuomotor task (post-test) showed a later time at PV in comparison to the pre-test session (Figure 3.7-15).

Table 3.7-10 Mean Training Peak Velocity Time values by Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	0.393 (0.039)	0.316, 0.471	-
Day 2	0.416 (0.040)	0.338, 0.495	0.526
Day 3	0.467 (0.041)	0.386, 0.548	**0.044***
Day 4	0.567 (0.042)	0.486, 0.649	**0.000***
Day 5	0.523 (0.046)	0.432, 0.613	**0.002***

* indicates p<0.05

3.7.13 Heading Error at 100ms

Heading Error at 100ms (HE) is the difference between desired heading and actual heading, calculated in a 10ms window centred 100ms following movement onset. Heading deviation was taken as a measure of the efficiency of *feedforward* processes, as it was assumed that adjustments of movement trajectory facilitated by visual feedback of the cursor were not possible prior to 100ms. Values closer to zero indicate lower heading error.

3.7.13.1 Motor Training Group

Left (training) limb: HE values were reduced for two targets at the post-intervention session: 'extension-radial' ($p=0.027$) and 'flexion-ulnar' ($p=0.004$), indicating a smaller heading error. At the retention session, HE at the 'flexion-ulnar' target remained smaller than pre-test HE ($p=0.004$). No other values were reliably different at post-test in comparison to HE values at pre-test at post-test.

Right (transfer) limb: At the post-training session, HE was larger for the right limb for two out of the eight targets. These were the 'flexion-radial ($p=0.032$) and 'extension-ulnar' ($p=0.015$) targets, signifying a greater heading error. The remaining six post-test target values were not reliably Changes in left-different from PV values at pre-test. At the retention test, no systematic differences in HE were observed in comparison to the pre-test.

3.7.13.2 Control Group:

For the control group, no systematic differences were observed across all targets at post-intervention for the left limb. At retention, the left limb HE was lower for the 'ulnar' target ($p=0.033$). For the right limb, PVT was lower at post-test for two targets: 'flexion-radial' ($p=0.033$) and 'extension-radial' ($p=0.009$); and for the 'flexion-radial' target, this difference was also seen at retention ($p=0.002$). No other reliable differences were observed between pre-test HE and post-test or retention-test HE amongst for either limb.

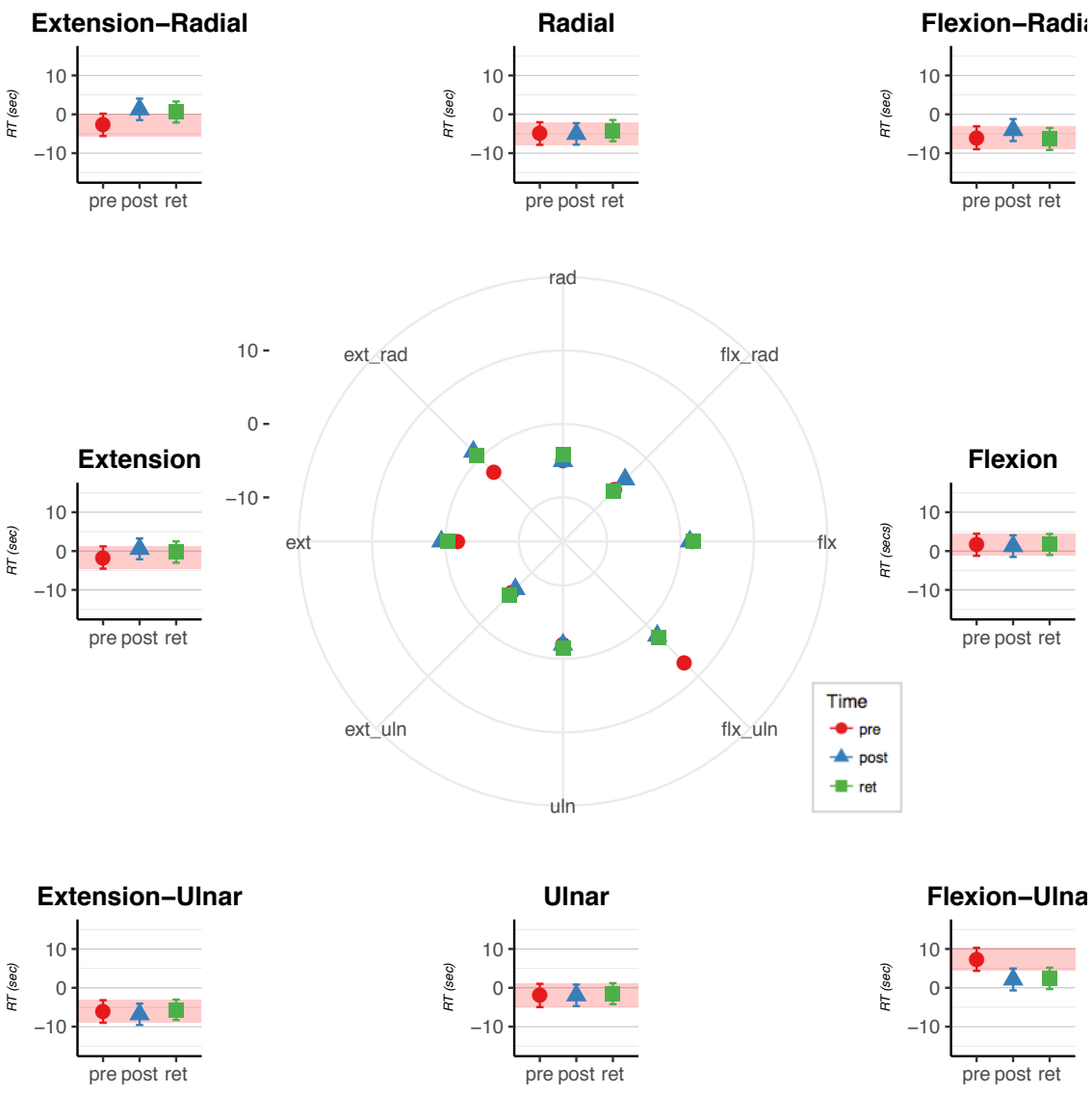

Figure 3.7-16 Heading error at 100ms for the training group left hand across testing sessions. HE is reduced (values closer to 0) at the extension-radial and flexion-ulnar targets at post-test. This reduction remained at the retention session for the flexion-ulnar target only. HE values closer to zero indicate less error. No other reliable differences in HE can be seen across sessions for the remaining targets.

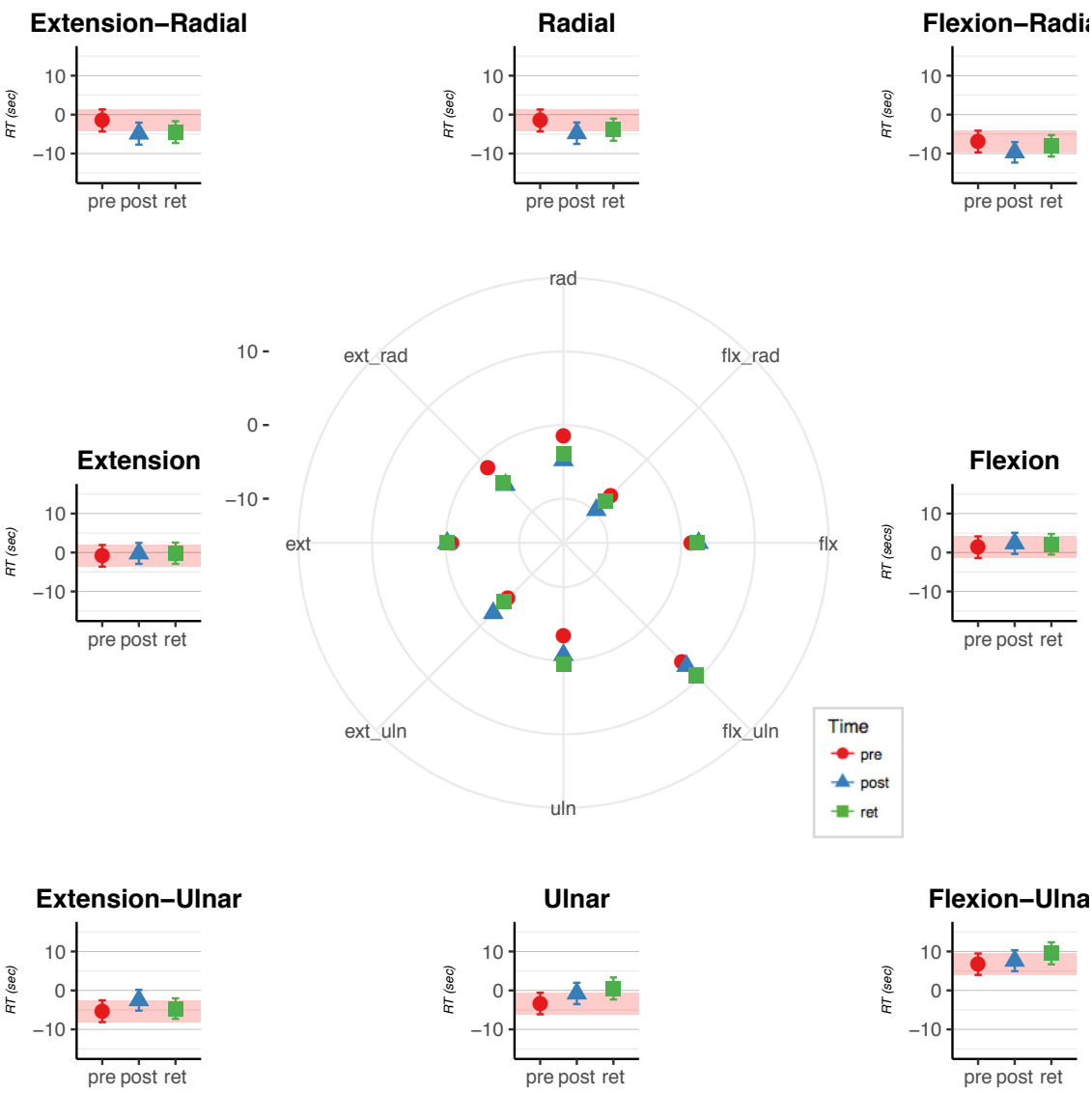

Figure 3.7-17 Heading error at 100ms for the control group left hand across testing sessions. No reliable differences in HE can be seen at the post-test session for any of the eight targets. For the ulnar target, a reduction in HE is seen at the retention session. No other systematic differences are seen across targets at retention.

Table 3.7-11 Pre –post and pre-retention contrasts for Heading Error at 100ms for the Training and Control Groups

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Left	***flx***	1.624	1.268	1.687	0.840	0.971	1.361	2.354	2.114	0.560	0.672
	flx_rad	-6.044	-4.051	-6.350	0.299	0.871	-6.911	-9.693	-8.005	0.108	0.536
	rad	-4.946	-5.051	-4.191	0.954	0.671	-1.507	-4.771	-3.879	0.069	0.192
	ext_rad	-2.717	1.273	0.579	**0.027***	0.066	-1.497	-4.873	-4.493	0.056	0.084
	ext	-1.665	0.562	-0.252	0.212	0.440	-0.852	-0.226	-0.175	0.721	0.708
	ext_uln	-6.093	-6.822	-5.650	0.689	0.801	-5.337	-2.516	-4.661	0.107	0.694
	uln	-1.966	-1.944	-1.512	0.990	0.803	-3.366	-0.780	0.505	0.138	**0.033***
	flx_uln	7.329	2.143	2.431	**0.004***	**0.007***	6.738	7.627	9.521	0.600	0.105

Table 3.7-11 Pre –post and pre-retention contrasts for Heading Error at 100ms for the Training and Control Groups (*continued)*

		Training					Control				
		Means			Contrast		Means			Contrast	
					Pre-Post	Pre-Ret				Pre-Post	Pre-Ret
Hand	**Target**	**Pre**	**Post**	**Retention**	***p-value***	***p-value***	**Pre**	**Post**	**Retention**	***p-value***	***p-value***
Right	***flx***	-1.180	-0.755	-0.284	0.817	0.620	-2.625	-1.160	-1.657	0.420	0.588
	flx_rad	3.221	7.126	6.650	**0.032***	0.058	2.658	6.629	8.562	**0.033***	**0.002***
	rad	4.203	6.475	4.189	0.199	0.994	3.166	4.806	6.092	0.364	0.108
	ext_rad	0.592	3.475	2.985	0.118	0.179	-1.469	3.254	1.741	**0.009***	0.071
	ext	-1.823	0.840	0.723	0.130	0.134	0.088	-0.208	-0.283	0.869	0.840
	ext_uln	-0.369	4.078	3.098	**0.015***	0.052	3.827	0.811	5.460	0.114	0.388
	uln	0.951	0.854	2.210	0.956	0.468	0.850	2.102	3.585	0.480	0.134
	flx_uln	-4.640	-2.901	-3.198	0.323	0.397	-1.613	0.758	-2.326	0.188	0.693

3.7.14 Intervention Group Heading Error at 100ms: Visuomotor Training

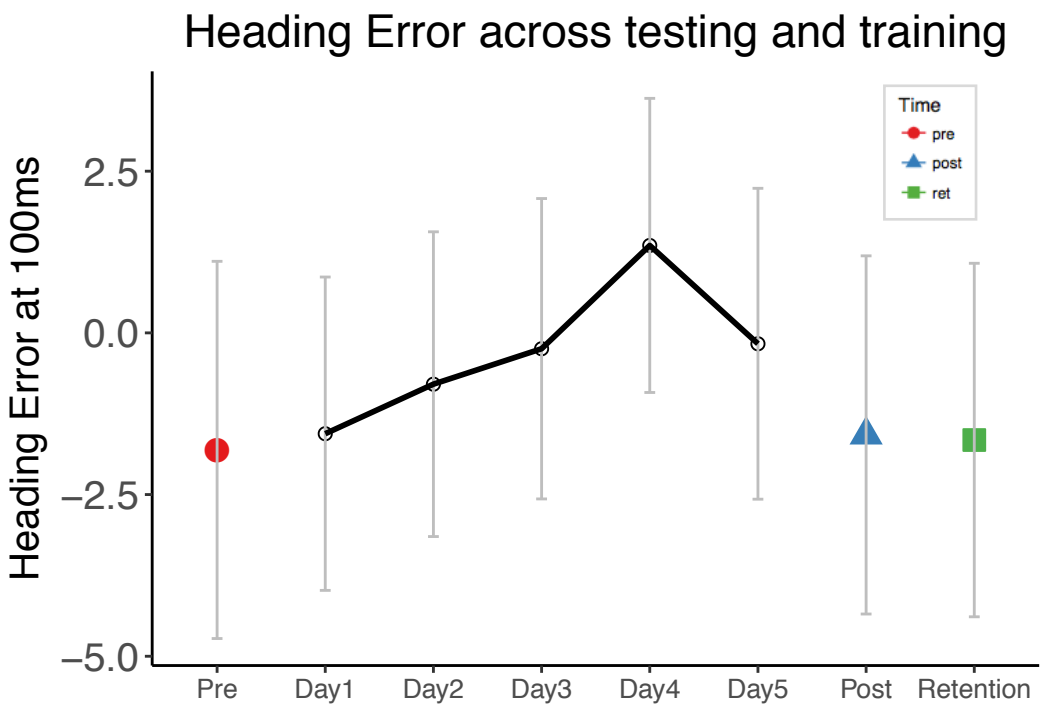

Figure 3.7-18 Changes in intervention group Heading Error across Testing Sessions and Training Days. The average HE across all targets is shown for each testing session, Pre, post and retention. In addition, the average HE across training day is shown in the centre of the figure, connected with a blue line. Mean HE on the visuomotor training task appears to get lower (closer to 0) from training Day 1 to training Day 5. No difference can be seen between HE at the pre-test, post-test and retention-test sessions.

No significant change in Heading Error at 100ms was observed on the visuomotor training task from Day 1 to Day 5 (p= 0.355). HE measures post-intervention were similar to those at pre-test (Figure 3.7-18).

Table 3.7-12 Mean Training Heading Error at 100ms values by Day.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day 1	-1.559 (1.236)	-3.982, 0.864	-
Day 2	-0.793 (1.202)	-3.149, 1.563	0.622
Day 3	-0.245 (1.185)	-2.568, 2.077	0.389
Day 4	1.352 (1.160)	-0.922, 3.626	**0.045***
Day 5	-0.168 (1.226)	-2.572, 2.235	0.355

* indicates p<0.05

3.7.15 Performance on the Visuomotor Training Task

Over the course of the 5 days of training, as task difficulty was increased by decreasing the target size, fewer targets were acquired by participants (Figure 3.7-19 below).

Figure 3.7-19 Pirate Plot showing Target Acquisition percentage by Training Day. Over the 5 days of training (Day 1 to Day 5), the target got progressively smaller, and the percentage of targets acquired by participants got smaller.

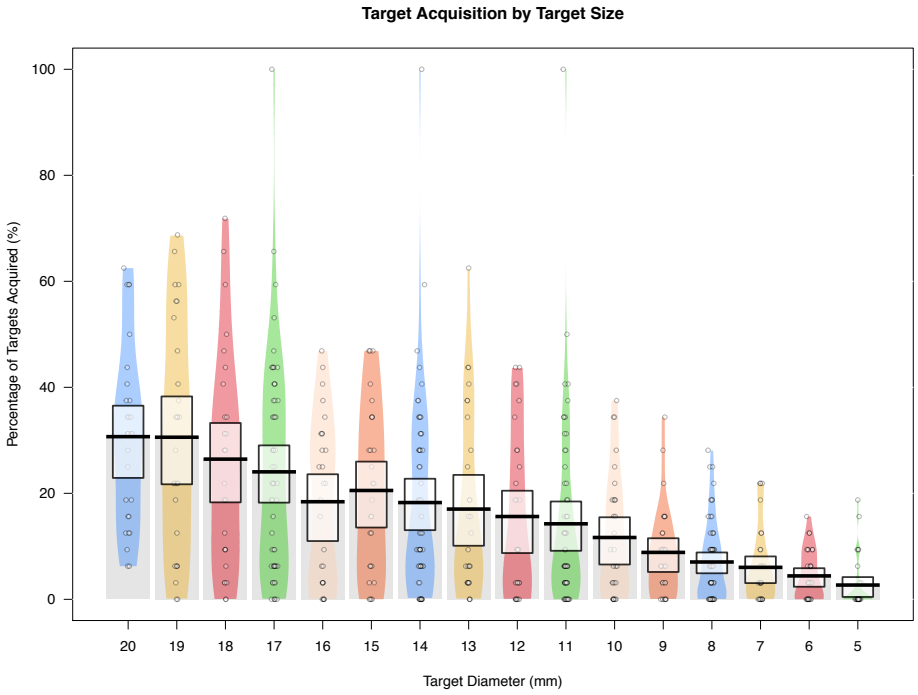

Figure 3.7-20 Pirate Plot showing the percentage of targets acquired at each target size (target diameter in mm). As target size decreased, the task became a lot more difficult, with fewer than 5% of targets acquired at the smallest target size (diameter = 5mm).

3.7.16 Change in Target Acquisition following Visuomotor Training

Change in Target Acquisition on the training task following the visuomotor training intervention was measured by calculating the percentage of targets acquired in Block 1, Day 1 and Block 5 on Day 5. In these two blocks, target size was equivalent and was set at the largest 'baseline' size (10 degrees). Thus, it was inferred that task difficulty was equivalent. This was to assess performance changes on the motor-coordination training task. As a core goal of the training task was to acquire targets, the percentage of targets acquired can be used to estimate overall performance in the task. Interestingly, at a group level, no significant changes were observed between the percentage of target acquisition from Day 1 to Day 5 (p=0.501) (Figure 3.7-21 below).

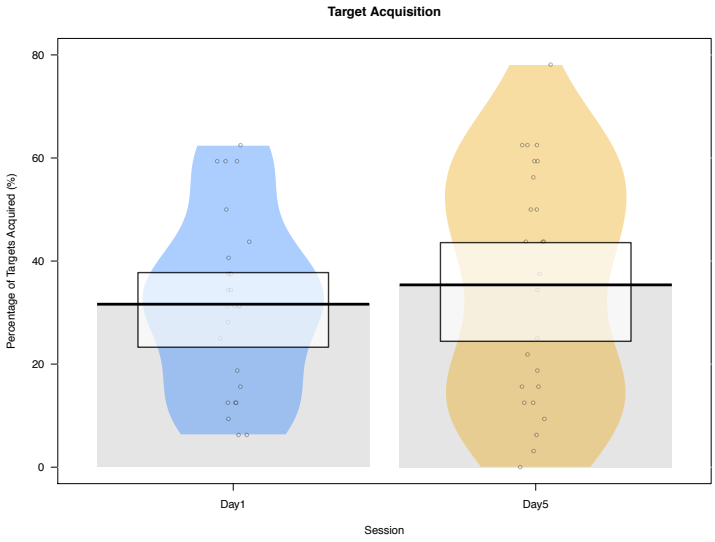

Figure 3.7-21 Change in Target Acquisition at the Baseline Visuomotor Task. The percentage of targets acquired did not change reliably following training on the coordination training task. However, the variation in the number of targets acquired was greater after training, indicated above by the spread of the bean in the Day 5 Block 5 group (yellow).

Table 3.7-13 Change in % Target Acquisition From Day 1 to Day 5, and Change Scores.

	Day1	***Day 5***	***Change***
Mean	31.62%	35.38%	+3.75%
Median	31.25%	37.5%	+6.25%
SD	17.41%	22.8%	29.08%
Min	6.25%	0%	-53.12%
Max	62.5%	78.12%	+50%

It is clear that there is a lot of variance between participants with respect to whether their Target Acquisition percentage improved or decreased over the course of training. This can be seen in the Histogram of the Change scores below (Figure 3.7-22) where positive numbers indicate an increase in the percentage of targets acquired, and negative scores a decrease.

This was evidently a very challenging training task, and at least with respect to using 'success in acquiring targets' as a metric of performance improvement, there was little manifestation of improvement. Indeed, the level of performance as captured by successful target acquisition was dictated to a large degree by the intrinsic difficulty of the task i.e. the size of the target (Figure 3.7-20). Nonetheless, it was clear that the participants adapted their movements in a number of ways during training, and that the influence of these adaptations was expressed during the assessments that took place during the following week, and ten days later.

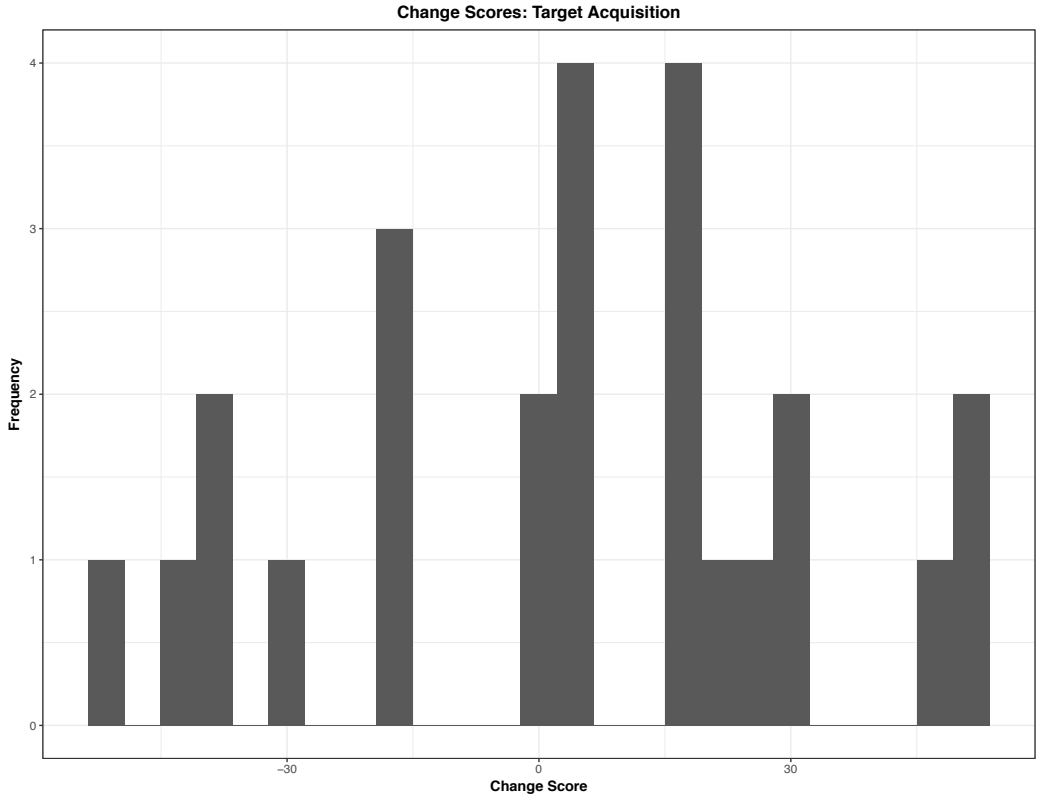

Figure 3.7-22 Histogram of change in the percentage of targets acquired from Day 1- Block 1, to Day 5-Block 5 (target size = baseline 10º/ 20mm). It is clear that the majority of participants did not improve, or only improved to a small degree, on the percentage of targets they acquired after the VM training, indicated by the highest frequency falling in the centre of the graph (centred on zero). However, it is interesting to note that in the performance of the exact same task on two occasions (start vs end of training), there are some participants who increased their percentage of targets acquired by 50%, and some who decreased their success rate by 50%.

3.8 Characterising adaptation to the Visuomotor Training Task

In order to derive an overall measure of the adaptation that occurred over the course of the training period, we first sought to determine separately for each target, the manner in which systematic variations (i.e. adaptations) in the five variables that characterised the movement trajectory (SAL, PD, PV, PVt, HE) accounted for changes in the primary measure of performance i.e. movement time. To this end, elastic-net penalised general linear regression was used to obtain an optimal set of weighted coefficients for the five predictor variables (i.e. SAL, PD, PV, PVt, HE). The residual representing the difference between the observed MT and the MT predicted by the model was obtained for each participant, and scaled by the intercept derived for the model (effectively the mean MT for each respective target). These scaled residuals were averaged across the eight targets to produce a single composite measure of adaptation for each participant.

3.8.1 Relationship between Visuomotor Task and Cognitive Results

To establish whether there were relationships between the measures of adaptation derived for the individual participants to the baseline motor task, and the degree of improvement exhibited by those individuals on the tests of cognitive function, statistical measures of association (Percentage Bend correlations (Wilcox, 2012) and robust linear regressions) were calculated. With a view to reducing the experiment-wise inflation of alpha that would otherwise arise as a result of conducting multiple inferential tests, these were generated only for assessments of cognitive function for which reliable changes from pre- to post-intervention had been obtained.

For the Motor Training group, there was an association between the VM adaptation measure manifested by individual participants, and the pre- to post-training percentage improvement in the WCST conceptual level responses (slope= -0.06575 , t =-2.309, df=, p=0.030, CI =-0.721, -0.002). No such reliable associations were present for any of the other improved cognitive outcome measures following training (i.e. Dual 2-Back Visual accuracy, Dual 2-back visual RT, WCST Total Errors, Table 3.8-1). In addition, no relationship was seen between cognitive outcome measures and adaptation to the VM for individuals in the active control group (Table 3.8-2).

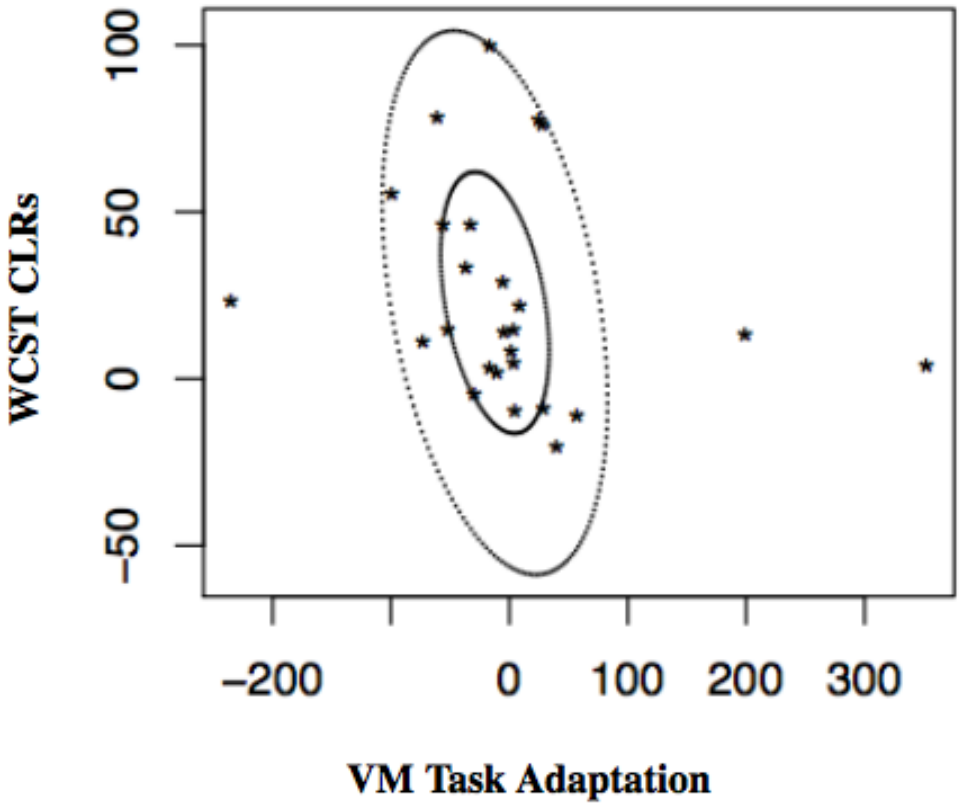

Figure 3.8-1- The percentage bend correlation between the VM Adaptation measure and the WCST. There was an association between the VM adaptation measure manifested by individual participants, and the pre- to post-training percentage improvement in the WCST conceptual level responses.

Table 3.8-1 Training Group: Percentage Bend Correlation Results for Pre-Post session associations between VM Adaptation and Cognitive Outcome Measures

Cognitive Task	PB Correlation	p (PB)	n	Lower CI (PB)	Upper CI (PB)
WCST CLRs	**-0.431**	**0.028**	26	-0.721	-0.002
WCST Total Error	0.145	0.480	26	-0.275	0.523
SART Omission Errors	0.069	0.738	26	-0.342	0.464
SART Commission Errors	-0.185	0.365	26	-0.581	0.322
Visuospatial 2-back Visual Accuracy	0.138	0.500	26	-0.222	0.468
Dual 2-back Visual RT	0.251	0.272	21	-0.244	0.686
Dual 2-back Visual Accuracy	-0.192	0.368	24	-0.521	0.220

Table 3.8-2 Control Group: Percentage Bend Correlation Results for Pre-post session associations between VM Adaptation and Cognitive Outcome Measures

Cognitive Task	PB Correlation	*p* (PB)	*n*	Lower CI (PB)	Upper CI (PB)
WCST CLRs	0.233	0.232	28	-0.211	0.612
WCST Total Error	-0.302	0.119	28	-0.619	0.089
SART Omission Errors	0.107	0.603	26	-0.299	0.576
SART Commission Errors	-0.090	0.663	26	-0.510	0.300
Visuospatial 2-back Visual Accuracy	0.344	0.073	28	-0.125	0.635
Dual 2-back Visual RT	0.121	0.601	21	-0.345	0.571
Dual 2-back Visual Accuracy	-0.198	0.322	27	-0.536	0.219

3.9 Discussion

Training on a wrist coordination task with deferred visual feedback gave rise to improvements in performance on tests of cognitive function. Moreover, such changes were not observed in an active control group. Tests that exhibited a reliable improvement in the motor training group only included the WCST, the Dual n-Back, and to a lesser extent, the Mental Rotation Task and the TMT.

For the WCST, the training group exhibited improvements in both the number of conceptual level responses (CLRs) and the total errors at the post-test session, both thought to reflect aspects of working memory (Kongs et al., 2000). No such reliable changes in performance were seen in the control group. This effect was also seen at retention. By retention, controls had improved on the task, but the effect size was small, whereas for the training group both at post and at retention, medium effects sizes were observed. It may be that the effects expressed at retention for the control group reflect practice effects associated with repetition of the tests of cognitive function. Furthermore, and most critically, the change in the level of CLRs for each individual was associated with the degree of adaptation to the baseline motor task. Such an association was not seen for the control group. While it is acknowledged that correlations in gain scores do not necessarily guarantee that transfer has occurred (Zelenski et al., 2014), it is nonetheless a remarkable finding that variation in the degree of adaptation to the motor training task was associated with the degree of improvement on the CLR component of the WCST. We are not aware of any such associations having been reported previously. In this context, it is worth emphasising that the training and assessment tasks used in the present study were somewhat unique in permitting not only tight control of the "dose" of coordination training that was administered, but also in providing means of quantifying precisely the adaptations in motor control that were brought about by that training. These attributes are not typically a characteristic of most motor fitness interventions, due at least in part to the nature of the training movements that have been employed (e.g. Moreau et al., 2015; Voelcker-Rehage et al., 2011; Johann et al., 2016; Ben Soussan et al., 2013; 2017).

It is also notable that the Mental Rotation RTs improved for the training group only, both at post-test and at retention, although this was just shy of the cut-off for a medium effect size. Previously it has been shown that training on certain motor tasks such as juggling or wrestling can lead to enhanced mental rotation performance (e.g. Jansen et al., 2009; Moreau et al., 2012; 2015). It has previously been recognised that

prior exposure to the mental rotation task can aid performance, even when different versions of the task are deployed (e.g. Peters, Laeng, Latham, Jackson, Zaiyouna et al., 1995), however it is seen here that only the group who took part in the deferred feedback visuomotor training task improved their post-test performance, and this suggests that the results are not as a result of practice effects. Improved RT performance on this task could indicate that participants were able to manipulate the mental image in a more efficient way, and could also indicate improved action selection when providing their response.

In the visuospatial n-Back task, control group participants exhibited improved accuracy performance on the 2-Back condition at post-test, and at retention both training and control groups showed an improvement in visual accuracy. For the Dual 2-back, the more difficult task, only the training group improved on 2-back visual accuracy post-test. This effect was not seen at retention. Improved performance on the most difficult task condition was only seen for the training group participants, and only in the visual accuracy condition. Whilst both interventions demanded visual attention and visuospatial 'working memory', in that participants needed to hold and manipulate information 'online' in order to improve task performance, this finding suggests that there was greater transfer from the coordination training intervention in processes required for more complex WM task variants. Potentially the need to hold information 'online' in this manner for its imminent use in action selection was more heavily dependent on spatial WM, and hence caused greater transfer on tasks measuring complex spatial WM.

For the Sustained Attention to Response Task, as in the first experiment, both groups reliably improved on the task by reducing the number of errors made in comparison to the pre-test both at post-test and at the retention (although only a small effect was seen for both groups at retention for the number of omission errors). This is perhaps an expected finding, due to the attentional demands of both the training and active control tasks, and the results obtained in Experiment 1. The 'active' control task had equivalent attentional demands, social contact and expectations of improvement to the training group (Boot, Simons, Stothart & Stutts, 2013), accomplished by training them on an adaptive task in identical settings to the training group. Both intervention conditions were required to concentrate intensely over four 4-minute blocks, similar to the four-minute SART task. It is likely, as in experiment 1, that both intervention tasks engaged sustained attention, leading to improvement on the SART. As noted previously, while a number of researchers have claimed that the SART is not susceptible to practice effects (Robertson et al., 1997; Di Rossa, 2014); given the pattern of outcomes obtained

in the present study – and in the absence of a no-contact control group, the intrusion of such effects cannot be ruled out.

The motor training intervention gave rise to changes in performance on the baseline motor task, with the training group exhibiting lower Path Deviation for the trained limb at the retention session, whereas this effect was not seen in controls. In addition, Peak Velocity was both lower and Time at Peak Velocity was later following motor training at both post-test and retention-test for the trained limb. No reliable changes were seen for the training group on measures of HE, MT or SAL. The control group, unsurprisingly, did not reliably exhibit any changes across any of the movement characteristics at the post-test or retention test.

In this task, as in the first experiment, there existed the opportunity for individual participants to vary the degree to which they achieved a balance between changes in motor characteristics (peak velocity, heading error, spectral arc length, path deviation and time at peak velocity) expressed ultimately in terms of movement time. Only among the motor training participants was lower Path Deviation and lower and later Peak Velocity observed, suggesting that after training, the nature of this balance (or a form of 'speed-accuracy' trade-off) was inclined toward accuracy. The "speed and accuracy trade-off'' (Fitts, 1954) is a well-known characteristic of fast target-directed movements, with movement speed decreasing as accuracy increases (see review by Plamondon & Alimi, 1997). As the motor training task we used was evidently a very challenging task, as seen in the low success rate of target acquisition both at the beginning and end of training, participants likely favoured slower movements that had a higher chance of accurately acquiring the target. Elsewhere it has been shown that older adults are more dependent on online visual feedback for correcting movements than younger adults (e.g. Yan, 2000), and perhaps in the absence of concurrent visual feedback, alternative strategies were needed to improve performance, such as emphasising lower Path Deviation. Perhaps encouraging older adults to engage in 'explicit' strategies in the motor task by providing post-trial feedback (e.g. Hinder et al., 2008; Bond & Taylor, 2015) led to transfer to the cognitive domain that similarly manifested as increases in accuracy performance, such as was exhibited on the WCST and the Dual 2-back task.

Interlimb transfer, expressed as change in the performance of the untrained limb, was measured to assess the generality of the adaptations that arose from the five days of training. It has been suggested that neural adaptations to unilateral training tasks subserve interlimb transfer of performance gains following training (e.g. Hinder et al. 2011; Hellebrandt, 1951; Lee et al., 2010). Despite the fact that there has been debate

concerning the nature of these adaptations (e.g. Ruddy et al., 2016; 2017), measures of transfer provide us with a means of examining the generality and robustness of learning, and we can infer from transfer that neural adaptations have occurred in response to the training demands. On the baseline VM task, along with decreases in Peak Velocity exhibited by the trained limb amongst participants in the motor training group, a decrease was seen in the untrained limb in Time at Peak Velocity at post-intervention. This suggested that there was inter-limb transfer of the PVT adaptations exhibited by the training limb. This effect was diminished for both the trained and untrained limb at retention. In addition, for the motor training group, coinciding with decreases in peak velocity for the trained limb, there was evidence, albeit to a lesser degree, of interlimb transfer resulting in lower PV at the post-test. It is apparent that changes in the right limb performance were observed among motor training participants only, and thus we can infer that neural adaptations following training occurred for motor-training participants. It has been shown that practice on a motor task leads to modification of the patterns of muscle synergies used, and gives rise to improved efficiency of motor commands that optimise the recruitment of such synergies (Carson & Riek, 2001). Accordingly, the demonstration of interlimb transfer is another level of support for the hypothesis that training on a complex coordination task can lead to neuronal adaptations, and it is our hypothesis that such changes are the basis upon which transfer to performance on the cognitive task was based.

From the notable variation in both the composite measure of adaptation to the VM task, and the individual differences in percentage change in the number of targets acquired following training, it is clear that the manner in which individual participants responded to training was heterogeneous. Moreover, we found evidence of a relationship between adaptation to the task and a measure of cognitive function (the WCST). These findings highlight the importance of assessing individual differences in responses to training. Previous attempts to quantify responses to cardiovascular interventions have utilised changes in maximal oxygen consumption (VO_2 max) for this purpose (e.g. Etnier et al., 2006), and often have not found reliable associations between VO_2 max and cognitive outcomes. Additional measures, such as changes in underlying movement characteristics, should be used in assessing individual response to physical training in to further explicate the nature of 'response' or adaptation to training. It is likely that this would lead to better understanding of the mechanisms leading to enhanced cognitive function. In this study, adaptation included characteristics separate from aerobic fitness, including PD, SAL, HE, PV and PVT. Furthermore, these characteristics varied in their

importance in the successful acquisition of different targets. So it is unlikely that 'superficial' measures of adaptation to physical activity that only measure change in one element of training can adequately capture the mechanisms mediating benefits seen in cognitive performance. In the future, further consideration should be given manner in which the expression of adaptations might vary across other motor tasks.

This study supports the hypothesis that motor training tasks involving 'explicit' movement planning and the precise coordination of muscle groups, such as required in rapid-aiming arm movement tasks with deferred visual feedback, can lead to improved performance on cognitive tasks in older adults. In the present study, the precise coordination of several muscles was required in order to generate motion in two degrees of freedom at the wrist joint (principally Flexor Carpi Radialis, Extensor Carpi Radialis, Flexion Carpi Ulnaris, and Extensor Carpi Ulnaris), and sophisticated neuromuscular control was required to accomplish the very precise movements (target zone was 1 degree of joint displacement) that were necessary to acquire the targets. In addition, in the absence of visual feedback, it is likely based on previous research on similar tasks (e.g. Hinder et al., 2008; Bond & Taylor, 2015), that participants were required to engage 'explicit' strategies for acquiring targets. We can speculate based on prior research that in order to improve performance or 'adapt' to the motor training task, widespread regions of the brain and central nervous system were engaged, and that this gave rise to 'transfer' to performance on cognitive tasks. Potential regions involved in this adaptation are likely to include areas traditionally classifieds as 'motor' regions, such as the cerebellum and basal ganglia, but also to regions that have traditionally been classified as 'higher-order' regions, such as the prefrontal cortices. Whilst we can only speculate that this is the case, future research using neuroimaging technologies could be engaged to explore the exact patterns of neural activation associated with training on coordination training tasks that, by deferral of visual feedback, encourage the use of 'explicit' strategies in achieving the goals of the task.

In conclusion, this experiment found that participants displayed improved scores on tests of cognitive function following training on a motor coordination task. These improvements were not reliably demonstrated by a tightly matched active control group. This study supports the hypothesis that motor training tasks involving 'explicit' movement planning and the integration of post-trial visual feedback, in addition to the precise coordination of muscle synergies, can lead to transfer to performance on cognitive tasks in older adults. It again provides support for the notion that the changes

in brain function induced by motor-coordination training extend beyond the classical motor network, to encompass regions that play a critical role in cognition.

Chapter 4 General Discussion

4.1 General discussion and closing remarks

The aim of this thesis was to explore:

(a) whether coordination training can be used to engender improved performance on tests of cognitive function in older adults.

(b) to elucidate the characteristics of coordination training that may be instrumental in bringing about such improvements.

As it has been appreciated throughout that in order to explore this relationship adequately, tight control of key variables is required, the experimental paradigm was based upon a class of coordinated (wrist) movement (centre-out target acquisition) tasks, that is already well described. In particular, this choice permitted the demands upon specific facets of motor control, and the dose of training, to be manipulated and monitored closely.

In Chapter 1, a review of the literature pertaining to cognitive enhancement was presented. Particular attention was paid to the ontologies that permeate contemporary cognitive science, and to the manner in which these have imposed restrictions upon the methods that have been applied in an attempt to enhance cognitive function in older people. It was proposed that an alternative 'enactive' ontology of cognition provides a context within which to understand improvements in executive functions brought about through physical activity, and that more generally this ontology provides a basis upon which to design interventions that have enhancement of cognitive function as their goal.

This analysis led to the formulation of a new research agenda that was given effect through two experimental studies. These used a carefully formulated and controlled methodology to explore whether training on a motor-coordination task could have a beneficial impact on "higher-order" cognitive processes. Comparisons were drawn with active control groups that engaged in otherwise equivalent tasks that had no requirement for the generation of goal-directed coordinated limb movements. In the first experimental study (Chapter 2), our hypothesis was that unilateral coordination training on a centre-out target acquisition task, in which participants received concurrent visual feedback of their movement trajectories, would lead to improvements in cognitive test performance. In the second experimental study (Chapter 3), a variant of the centre-out target acquisition task was employed, which was designed to place additional emphasis

upon the requirement for feedforward planning. Participants received deferred visual feedback of their movement trajectories during a motor task that was otherwise equivalent to that used in the previous study. It was assumed that this manipulation would promote the use of 'explicit' learning strategies on the part of the participants. We hypothesised that training on this task would lead to improved scores on tests of cognitive function. In the context of both studies, we further attempted to identify the nature of the adaptations in motor control that were associated with observed changes in cognitive function.

4.2 Summary of empirical findings

In Experiment 1 (Chapter 2), we found some evidence that unilateral motor training led to differential improvements on cognitive measures in comparison to an active control group. Only participants who engaged in the motor intervention improved on both motor and cognitive subtasks of the Choice Reaction Time task, and Auditory Reaction Time in the Dual 1-back task. Both groups improved performance on the Sustained Attention to Response Task. In addition, five days of training on the motor training task gave rise to changes in parameters that characterise the movements that were generated in the target acquisition task. When assessed following the training period, movement times were shorter and path deviations lower than prior to training. No corresponding changes in performance were observed for the control group. In addition, for the participants who engaged in the motor training intervention, a degree of interlimb transfer of skill was observed, with the untrained limb showing decreased peak velocity of movement post-training.

A composite measure of adaptation was derived to assess changes (from pre- to post-training) in motor control expressed in the context of the target acquisition task. However, no associations were found between this measure and the observed changes in cognitive outcome measures.

In Experiment 2 (Chapter 3), it was revealed that following a period of unilateral coordination training in which visual feedback was deferred, participants systematically improved performance on the Wisconsin Card Sorting Task, purportedly a measure of cognitive flexibility and working memory - expressed as increases in the number of conceptual level responses and decreases in the total errors. In addition, some small

improvements were seen in the performance of the TMT and Mental Rotation tasks that were not exhibited by participants in the control group.

Motor training group participants carried out five days of training on the motor task, in which visual feedback of movement trajectories was deferred until after the movement was completed, and target size was progressively diminished to increase task difficulty. Firstly, the change in the percentage of targets acquired between the first block of training on Day 1, and the final block of the task on Day 5 (in which the target size matched the first block on Day 1) was calculated. These tasks were identical in nature. Percentage change in target acquisition varied greatly between individuals, and overall no improvement was observed.

In addition, training on the deferred feedback motor training task led to changes in performance on the visual assessment task captured at the post-test and retention-test sessions. Individuals who engaged in the motor training intervention generated movements (of the trained limb) that were characterised by Path Deviation values that were lower in the retention session, than prior to training. This effect was not seen in controls. Peak Velocity was both lower and Time at Peak Velocity was later following motor training at both post-test and retention-test sessions for the trained limb. The control group did not reliably exhibit any changes across any of the movement characteristics at the post-test or retention test.

For the individuals who engaged in the motor training intervention, interlimb transfer was exhibited, with a decrease in Peak Velocity and Time at Peak Velocity seen in the untrained limb at the post-test session.

Finally, a composite measure of adaptation to the baseline motor task was derived to assess changes in motor control expressed following the training period. Amongst the participants who were engaged in the motor training task, an association was revealed between the level of adaptation to training the task and a measure of cognitive function that exhibited improvement following training: conceptual level responses on the WCST. No such association was seen for the control group participants.

4.3 General discussion of findings in relation to existing literature

The methodology used within this thesis provides a means of measuring in a precise fashion the adaptation to a period of motor training. This has not previously been

possible in other motor-fitness interventions which have employed complex 'whole-body' movement training programmes (e.g. Moreau et al., 2015). The use of a motor training paradigm in which participants were trained on a 2 degree-of-freedom centre-out target acquisition task provided us with the means to ensure the dose of training across individual participants was equivalent, and to measure the changes in the underlying movement characteristics associated with adaptation to the training task. This innovative design gave us the unique opportunity to derive a composite measure of adaptation to the training task. We were then able to explore associations between this measure of adaptation to the motor training task and performance improvement on the cognitive measures. In Experiment 2, for individuals who engaged in the motor training intervention, we found an association between individual changes in performance on the visuomotor assessment task and the level of performance improvement on a subtask of the WCST. Previously, motor-fitness interventions have not been able to quantify response to training in such a way due to the many degrees of freedom involved in the motor-fitness training paradigms they employed (e.g. Moreau et al., 2015; Forte et al., 2013; Berryman et al., 2014; Voelcker-Rehage et al., 2011). In addition, due to the complexity of the tasks employed in these interventions, such as 'designed sport' (Moreau et al., 2015) or Quadrato Motor Training (Ben-Soussan et al., 2013), they have not been able to ensure that dose of training was exactly equivalent across participants.

The experimental findings presented in this thesis have provided support for the conjecture that components of physical activity interventions additional to increased cardiorespiratory or 'aerobic' capacity can lead to benefits in cognitive function (eg. Voelcker-Rehage, 2011; Diamond et al., 2016). Inconclusive results are presently seen in reviews of the effects of aerobic physical activity interventions on cognitive performance (e.g. Angevaren et al., 2008; Smith et al., 2011), with some showing positive effects of physical activity, and others finding null effects on the same cognitive tasks. Even among meta-analyses finding positive 'transfer' from the physical activity interventions to the cognitive domain, associations between individual level of 'improvement' on the training measure and cognitive outcomes have not been demonstrated. For example, a meta-regression of studies showing improved cognitive performance after aerobic physical activity interventions found no reliable relationship between changes in individual level of cardiorespiratory fitness (i.e. maximal oxygen uptake) and cognitive function (e.g. Etnier et al., 2006). Thus, it may be that other mechanisms are mediating the relationship between Physical Activity interventions and enhanced cognitive function, such as elements of motor control that are also engaged in

Physical Activity interventions. Indeed, it has recently been suggested that physical activity interventions need to have a complex 'motor learning' element in order for transfer to the 'cognitive' domain to be observed (e.g. Diamond, 2016; Moreau et al., 2014). In the second experiment presented in this thesis, in which participants trained on a motor task that manipulated the visual feedback in order to engage 'explicit' learning strategies, it was found that motor training led to improved performance on measures of 'executive function', namely, the WCST, and to a lesser degree improved performance on the Mental Rotation Task and visual accuracy on the Dual 2-back task.

Of major concern pertaining to the domain of cognitive training, in which attempts to enhance function are made by engaging people repeatedly on specific cognitive tasks, is that the benefits from training on one task do not generalise to unrelated, structurally different tasks (e.g. Melby-Lervag, Redick & Hume, 2016; Morrison & Chien, 2011; Shipstead et al., 2012). Such 'wide' transfer, from the trained task to untrained tasks, has yet to be unequivocally demonstrated as an outcome of cognitive training tasks (e.g. Lampit et al., 2014). It has been proposed that transfer from trained to untrained tasks is caused by the activation of shared neural mechanisms (Jonides, 2004). Whilst in the present study, participants exhibited improved performance on some measures of executive function following motor training interventions, the interpretation of whether the effects seen constitute 'near' transfer or 'wide' transfer is dependent on how wide transfer is defined. In the cognitive training literature, near transfer is defined as improvement on tasks that are 'structurally similar' in nature to the task used in training, whereas 'wide' or 'far' transfer is when improvements are seen on tasks that have not been trained. Typically, far transfer is measured with cognitive tests that are 'structurally different' to the trained task.

In the two experiments derived in this thesis, certain RT measures in cognitive tasks improved across both experiments. In the first experiment, individuals who engaged in the motor training task exhibited latencies for both the "cognitive" and "motor" elements of the CRT task that were shorter during the post-intervention assessment than those recorded prior to the intervention. In contrast, individuals in the active control group did not exhibit such changes in performance. In addition, in the second experiment, for participants who engaged in the motor training intervention, RT measures were lower on the Mental Rotation task at the post-test session.

Firstly, it is not possible to reliably state that reductions in RT measures (such as those seen for the training group on the CRT in Experiment 1) are attributable to changes in some 'cognitive' aspects of motor function. Potentially, RT improvements could be

arising from motor responses engaged in the particular mode of intervention, as a manifestation of 'near' transfer between training and the cognitive outcome measures that share common elements. In the first experiment, participants who engaged in the motor training intervention exhibited reductions in both Movement Time and Reaction Time (Appendix 2) on the post-test visuomotor assessment task. As the motor training task emphasised speed of execution, with the participants encouraged to hit targets appearing onscreen as quickly and accurately as possible, it is probable that the decreases in RT measures on the CRT are manifestations of 'near' transfer between tasks that share common (motor) elements, caused by the activation of shared neural mechanisms (Jonides, 2004). However, in the second experiment, participants who engaged in the motor training task (with deferred visual feedback) did not exhibit reductions in Movement Time or Reaction Time on the visuomotor assessment task at the post-test session. Yet they did exhibit improved RT scores on the Mental Rotation task. Thus, it is more likely that transfer in this instance occurred on a wider scale.

These findings highlight the importance in appropriately (and conservatively) interpreting some of the measures used customarily to assess "cognitive function", both in the context of interventions that employ physical responses, and in those that do not. Indeed, many "physical activity" interventions have similar 'movement' task characteristics to those that characterise several cognitive assessment tools (Cremen & Carson, 2017). The implications of this are that the interpretations that can be drawn from cognitive outcome measures are limited and often we cannot reliably state that 'wide' transfer to a task very different from the training task has occurred.

Indeed, this draws into question the nature of purported measures of cognitive function. Meta-analytic evidence derived from brain imaging research has shown that common tasks purporting to measure executive functions, i.e. working memory, inhibitory control and cognitive flexibility, most frequently engage broadly distributed brain regions (Uttal, 2013; Niendem et al., 2012), and frequently engagement of the classical motor networks (Cremen & Carson, 2017; Uttal, 2013). Previous analyses have suggested that the executive control nominally sampled by certain cognitive tests that have a Reaction Time demand, as does the CRT task used in this thesis, may represent an evolutionary extension of the frontal cortex-basal ganglia loops that guide resolution of (motor) response conflict. The role of the supporting neural mechanisms extends to a range of processes including the reorienting of attention and the updating of WM (Neubert et al., 2013). Therefore, it is not possible to conclude that improved performance on CRT measures constitutes 'far' transfer to a 'cognitive' task. Again, the

division of measures into 'cognitive' and 'motor' tasks is problematic, and as it becomes ever more apparent that cognitive and motor functions cannot fully be understood in isolation, this false dichotomy needs to be amended. Perhaps with a wider adoption of an 'enactive' model of the brain and cognition, neural states would be determined "by their functional role in the guidance of action, not by a mapping to a stimulus domain" (Engel et al., 2013, p.207), as is often the modus operandi in current representationalist accounts of the brain and cognition. This would allow for clearer interpretation of improvements on cognitive measures following interventions aiming to enhance cognitive function, and potentially more conclusive results concerning what constitutes 'near' or 'wide' transfer.

'Explicit' strategies in sensorimotor adaptation paradigms, which have recently been suggested to constitute the 'fast' or early stage of sensorimotor adaptation, are thought to be mediated by cortico-cerebellar networks and parietal brain regions (Flament et al., 1996; Seidler & Noll, 2008). 'Explicit' strategies have been framed as the 'cognitive' components involved in adapting to a motor task (McDougle, Ivry & Taylor, 2016). It is notable that in the second experiment presented in this thesis, changing motor training task parameters by deferring visual feedback in order to emphasise 'explicit' learning strategies, led to more compelling improvements in EFs for participants engaging in the motor training intervention. Based on previous work exploring 'explicit' strategies in adaptation to visual tasks (e.g. Bond & Taylor, 2015), it is likely that engaging in motor training activities that engage these 'explicit' strategies requires a deeper level of feedforward planning. In contrast, in experiment 1, the motor training task emphasised the 'automatic' or 'implicit' updating of internal models using 'sensory-prediction errors', for example, the disparity between predicted and actual cursor position that was used to improve performance (e.g. Wolpert et al., 1998). The 'explicit' learning strategies emphasised the strategic and conscious planning of action sequences, and this led to better performance on cognitive tasks that similarly required strategic planning of actions in response to visual stimuli, namely the WCST, the TMT and the Mental Rotation task. On the other hand, the improvements seen in experiment 1 were shown in a simple Choice Reaction Time task, that, as we have outlined, cannot readily be described as involving 'higher-order' cognitive processes (i.e. complex or strategic action planning). This is a very interesting finding, as it enables us to hypothesise that in order for greater 'cognitive' benefits to occur, motor tasks involving 'explicit' learning strategies should be engaged. However, it must be noted that due to the differences in the outcome measures used in the two tasks, direct comparison between

the two experiments is not possible or reliable. Future research should test this hypothesis more directly, comparing groups carrying out motor training programs that differentially emphasise 'implicit' and 'explicit' learning strategies.

The finding presented in this thesis, in particular in the second experiment, are in line with action-oriented theories of cognition, in that training on an action based task led to improvements in 'cognitive' function. The findings lend support to the hypothesis that the changes in brain function induced by motor-coordination training extend beyond the classical motor network, to encompass regions that play a critical role in cognition. Training on a 'motor' task led to improvements on the WCST, a commonly used test of executive function. The WCST was previously conceptualised as heavily dependent on frontal lobe function (e.g. Milner, 1963), however, as is now being shown for many tests of cognitive function, brain imaging data has illustrated that widespread activation across both frontal and non-frontal regions is observed during WCST performance in healthy controls (Nyhus & Barcelo, 2009). Thus, it is hypothesised that shared neural activations underlie the improvements observed in both the visuomotor assessment task and the WCST.

4.4 Limitations and future directions

Given that the behavioural outcomes indicate that changes have occurred both in performance on 'motor' tasks and 'cognitive' tasks, we have some grounds to make the case for shared neural activations common to both sets of tasks. For example, we can hypothesise, based on previous research, that changes following motor training engage widespread networks in the brain, including classical 'motor' networks such as the cerebellum (e.g. Butcher et al., 2017) and basal ganglia (Houk et al., 2007) and regions classically associated with 'cognitive' performance, such as the PFC and DLPFC. In the context of the two experiments presented in this thesis, we can speculate that the motor training task utilised in Experiment 1 is thought to have engaged 'implicit' learning processes that more heavily engaged the classical motor networks. However, it is likely that due to the manipulation of visual feedback in the second experiment, 'explicit' strategies were used in performance of the task, which are thought to engage wider cortico-cerebellar networks (e.g. Butcher et al., 2017). However, additional research would be needed to confirm if this were, in fact, the case. This could be examined further by using in-vivo constrained spherical deconvolution techniques which have previously been used to show that individual variations in white matter connectivity predict the transfer of learning that is manifested following a period of motor training (e.g. Ruddy et al., 2016). Functional neuroimaging techniques might also be used to explore whether differences in regional connectivity between participants engaging in 'implicit' and 'explicit' learning strategies are predictive of the observed patterns of transfer to the cognitive domain.

It was shown in Experiment 2 that there was huge inter-individual variation in at least one measure of performance the task. For example, target acquisition was a central goal of the task, and it was shown that as the target size progressively diminished, the percentage of targets acquired decreased: at the largest target size, the average percentage of targets acquired was 32%, whereas in the most difficult condition, the average percentage acquired was only 4%. Evidently this was a very difficult task, especially in the later stages of training. However, after the final training block, when target size was increased back to the initial 'largest' size, the average percentage of targets acquired was not reliably different from Day 1 percentages (an increase of less than 4%). At a group level, this would appear to show that no improvement on the task occurred. However, when looking at individual percentage change on the two equivalent tasks (Day 1 vs Day 5), there was enormous variation in performance (see Figure 3.7-22). The reasons

underlying these differences in performance need to be more fully understood. It is probable that 'adaptation' strategies used during the motor training were more efficient for some participants over others. Further, these results could potentially be due to motivational factors associated with the task. Anecdotally, it was recognised by the trainers carrying out the individual training sessions, that over the course of the training intervention, some participants (both in training and control groups) thoroughly enjoyed the experience and engaged fully with the training, whereas others seemed less motivated to perform at their highest level once the task got too difficult. Extensive research has been carried out in the domain of training motivation (for a meta-analysis of 20 years of training motivation, see Colquitt, LePine & Noe, 2002), and has shown that training motivation can be responsible for variance in learning outcomes. A meta-analysis by Colquitt et al. (2002) found that many individual characteristics may predict training motivation, including age, cognitive ability, locus of control and anxiety. However, training motivation was found to be a better predictor of training outcomes than cognitive ability. As we did not assess participants individual levels of motivation to improve performance on the task, we cannot state the cause of the variability in performance change, but in future research in this domain, subjective measures of task engagement could be obtained following training sessions by assessing participants' enjoyment or levels of motivation. This may allow for experimental control in individual engagement with the task.

On a somewhat related note, it has been suggested that complex 'whole-body' training activities may be more 'ecologically valid' than lab-based training interventions (e.g. Moreau, 2014). Ecological validity is frequently defined as the extent to which results obtained in controlled experimental settings apply to real-world naturalistic settings (Tupper and Cicerone, 1990). However, it has been noted elsewhere that complex movement training tasks performed in open environments are very difficult to control due to the increased degrees of freedom in responses (Moreau and Conway, 2014). Whilst some might argue that the current approach has limited ecological validity, as training was limited to a 2 degree of freedom movement task in a laboratory setting, it is maintained that such specificity is in fact a strength of our methodology. As is clear from the two studies described out in this thesis, tightly controlled movement tasks may provide insight into many important factors in training interventions, such as individual differences in adaptation to training, and the associations between the training and improved performance on the cognitive outcome measure. Nonetheless, it is recognised that experiments carried out in more naturalistic settings have alternative benefits. Future

attempts to explore motor training could exploit emerging technologies in order to improve ecological validity and measure movement in naturalistic settings. The development of controllable virtual environments, that allow for greater complexity of movement, is one potential method for this. Especially promising are the development of affordable motion-capture devices, such as gesture control devices (e.g. Myo Gesture Control Armband, Figure 4.4-1) or video game consoles (e.g., Microsoft Kinect).

Figure 4.4-1 Motion capture devices, such as the Myo arm band (left) and virtual reality headsets, are technologies that permit complex movements in controllable virtual environments.

Figure 4.4-2 A patient carries out a physical therapy regimen from their home using Microsoft Kinect. Photo taken from: https://blogs.msdn.microsoft.com/kinectforwindows/2014/12/04/intel-ge-care-innovations-uses-kinect-solution-to-help-elderly-patients/

Individual differences should be further explored and emphasised in intervention studies aiming to enhance cognitive function. It is evident from the second experiment presented in this thesis that response to the intervention varied markedly. Task difficulty could be modified on an individual basis to better suit the capabilities of individual

participants. Tailoring to individual needs is likely to be a very important issue in future research in this domain, especially considering the potential variance in capabilities between a 65-year-old and a 90-year-old, which at present are often simply categorised as 'older adults'. It has been demonstrated that there exist individual trajectories for the structural and functional integrity of individual brains that are not accounted for by chronological age (Raz et al., 2005; 2010). Brain imaging methodologies could be harnessed to explore the neural substrates that constrain individual capacity for learning and transfer (e.g. Ruddy et al., 2016). It has also been recognised that declining functions begin at a much younger age than 65, and studies exploring middle-adulthood (i.e. 40-60 years) are few (Seidler, 2012), despite the apparent presence of functional declines in this age-group. Exploring the individual trajectories of decline and capacity for transfer should be explored from mid-adulthood.

On a related note, leveraging new motion-capture technologies and marrying them with motor training programmes (such as those described in the experiments in this thesis) provide a potential avenue for the creation of systems for the personalised assessment, maintenance and promotion of cognitive health in older adults. As the costs associated with such technologies decrease, and the knowledge relating motor training to cognitive enhancement increases, such systems could eventually be suitable for widespread adoption in the home and community settings. The specific research described in this thesis represents a possible preliminary step in the marrying of motion-capture technology with knowledge of the physiological and psychological principles that determine the mechanisms underlying transfer of benefits from motor training programs to the cognitive domain.

4.5 Concluding remarks

The original contributions arising from the investigations presented in this thesis are firstly, the demonstration that training on a motor task, in this instance unilateral coordinated movement training on a centre-out target acquisition task, can lead to improvements in cognitive task performance. The motor training and motor assessment tasks used in the present study were somewhat unique in permitting not only tight control of the "dose" of coordination training that was administered, but also in providing means of quantifying precisely the adaptations in motor control that were brought about by that training. Secondly, through tight experimental control, it was demonstrated that the individual level of adaptation to a motor training task, that provided deferred visual feedback, was associated with change in performance on a specific cognitive measure. We are not aware of any such associations having been reported previously. The results presented herein are thus a valuable addition to the existing knowledge base concerning cognitive enhancement in older adults, and will be instrumental in informing further investigation.

References

Alvarez, J. A., and Emory, E. (2006). Executive function and the frontal lobes: a meta-analytic review. *Neuropsychol. Rev. 16*, 17–42. doi: 10.1007/s11065-006-9002-x

Anderson, E. S., Winett, R. A., Wojcik, J. R., & Williams, D. M. (2010). Social cognitive mediators of change in a group randomized nutrition and physical activity intervention: social support, self-efficacy, outcome expectations and self-regulation in the guide-to-health trial. *Journal of Health Psychology*, 15(1), 21-32.

Anderson, J. R. (2007). *How can the human mind occur in the physical universe?* Oxford: Oxford University Press.

Anderson, M. C., & Levy, B. J. (2009). Suppressing unwanted memories. *Current Directions in Psychological Science*, *18*(4), 189-194.

Anderson, M. L. (2010). Neural reuse: A fundamental organizational principle of the brain. *Behavioral and brain sciences*, *33*(4), 245-266.

Anderson, M. L. (2014). *After phrenology*. MIT Press.

Anderson, M. L. (2016). Précis of After Phrenology: Neural Reuse and the Interactive Brain. *The Behavioral and Brain Sciences, 39*, e120. http://doi.org/10.1017/S0140525X15000631

Anderson, M. L., & Penner-Wilger, M. (2013). Neural reuse in the evolution and development of the brain: Evidence for developmental homology? *Developmental Psychobiology*, *55*(1), 42–51.

Anderson, M., & Chemero, A. (2016). The Brain Evolved to Guide Action. *The Wiley Handbook of Evolutionary Neuroscience*, 1-20.

Angevaren, M., Aufdemkampe, G., Verhaar, H. J. J., Aleman, A. & Vanhees, L. Physical activity and enhanced fitness to improve cognitive function in older people. *Cochrane.Database.Syst.Rev.* 1–73 (2008).

Anguera, J. A., Boccanfuso, J., Rintoul, J. L., Al-Hashimi, O., Faraji, F., Janowich, J., ... & Gazzaley, A. (2013). Video game training enhances cognitive control in older adults. *Nature, 501*(7465), 97-101.

Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2010). Contributions of spatial working memory to visuomotor learning. *Journal of cognitive neuroscience*, *22*(9), 1917-1930.

Anguera, J. A., Reuter-Lorenz, P. A., Willingham, D. T., & Seidler, R. D. (2011). Failure to engage spatial working memory contributes to age-related declines in visuomotor learning. *Journal of cognitive neuroscience*, *23*(1), 11-25.

Anguera, J., Russell, C., Noll, D., & Seidler, R. (2007). Neural correlates associated with intermanual transfer of sensorimotor adaptation. *Brain Res, 1185*, 136-151.

Arbuthnott, K., & Frank, J. (2000). Trail making test, part B as a measure of executive control: validation using a set-switching paradigm. *Journal of clinical and experimental neuropsychology, 22*(4), 518-528.

Ardila, A., Bernal, B., & Rosselli, M. (2017). Executive Functions Brain System: An Activation Likelihood Estimation Meta-analytic Study. *Archives of Clinical Neuropsychology*, 1-27.

Audiffren, M., Tomporowski, P. D., & Zagrodnik, J. (2009). Acute aerobic exercise and information processing: modulation of executive control in a Random Number Generation task. *Acta psychologica*, *132*(1), 85-95.

Auyeung, T. W., Lee, J. S. W., Kwok, T., & Woo, J. (2011). Physical frailty predicts future cognitive decline - a four-year prospective study in 2737 cognitively normal older adults. *The Journal of Nutrition, Health & Aging, 15*(8), 690--694.

Baddeley, A. D., & Hitch, G. J. (1994). Developments in the concept of working memory. *Neuropsychology*, 8(4), 485-493.

Baezner, H., Blahak, C., Poggesi, A., Pantoni, L., Inzitari, D., Chabriat, H., et al. (2008). Association of gait and balance disorders with age-related white matter changes: the LADIS study. *Neurology*, *70*(12), 935–942. http://doi.org/10.1212/01.wnl.0000305959.46197.e6

Bailey, C.E., (2007). Cognitive accuracy and intelligent executive function in the brain and in business. *Ann. N.Y. Acad. Sci. 1118*, 122–141, http://dx.doi.org/10.1196/annals.1412.011.

Balasubramanian, S., Melendez-Calderon, A., & Burdet, E. (2012). A robust and sensitive metric for quantifying movement smoothness. *IEEE transactions on biomedical engineering*, *59*(8), 2126-2136.

Balasubramanian, S., Melendez-Calderon, A., Roby-Brami, A., & Burdet, E. (2015). On the analysis of movement smoothness. *Journal of neuroengineering and rehabilitation*, *12*(1), 112.

Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: A new window to the study of cognitive aging? *Psychology and Aging, 12*(1), 12-21.

Bamidis, P. D., Vivas, A. B., Styliadis, C., Frantzidis, C., Klados, M., Schlee, W., ... & Papageorgiou, S. G. (2014). A review of physical and cognitive interventions in aging. *Neuroscience & Biobehavioral Reviews, 44*, 206-220. http://doi.org/10.1016/j.neubiorev.2014.03.019

Ben-Soussan T. D., Glicksohn, J., Goldstein, A., Berkovich-Ohana, A., Donchin, O. (2013). Into the Square and out of the Box: The effects of Quadrato Motor Training on Creativity and Alpha Coherence. *PLoS ONE, 8*(1): e55023. doi:10.1371/journal.pone.0055023

Ben-Soussan, T. D., Piervincenzi, C., Venditti, S., Verdone, L., Caserta, M., and Carducci, F. (2015). Increased cerebellar volume and BDNF level following quadrato motor training. *Synapse 69*, 1–6. doi: 10.1002/syn.21787

Benedict, R. H. B., & Zgaljardic, D. J. (1998). Practice effects during repeated administrations of memory tests with and without alternate forms. *Journal of Clinical and Experimental Neuropsychology*, *20*, 339-353.

Bernard, J. A., & Seidler, R. D. (2014). Moving forward: Age effects on the cerebellum underlie cognitive and motor declines. *Neuroscience & Biobehavioral Reviews, 42*, 193-207.

Bernstein, Nikolai (1967). *The Coordination and Regulation of Movements*. Oxford: Pergamon Press.

Berryman, N., Bherer, L., Nadeau, S., Lauzière, S., Lehr, L., Bobeuf, F., et al. (2014). Multiple roads lead to Rome: combined high-intensity aerobic and strength training vs. gross motor activities leads to equivalent improvement in executive functions in a cohort of healthy older adults. *Age, 36*(5), 9710.

Best, J.R., 2010. Effects of physical activity on children's executive function: contributions of experimental research on aerobic exercise. *Dev. Rev. 30*, 331–351.

Bezerra, A. B. C., Coutinho, E. S. F., Barca, M. L., Engedal, K., Engelhardt, E., & Laks, J. (2012). School attainment in childhood is an independent risk factor of dementia in late life: results from a Brazilian sample. *International Psychogeriatrics, 24*(01), 55-61.

Bherer, L., Erickson, K. I., & Liu-Ambrose, T. (2013). A review of the effects of physical activity and exercise on cognitive and brain functions in older adults. *Journal of aging research*, *2013*. doi:10.1155/2013/657508.

Bishop, N. A., Lu, T., & Yankner, B. A. (2010). Neural mechanisms of ageing and cognitive decline. *Nature, 464*(7288), 529-535.

Block, N. (2008, October). Consciousness and cognitive access. In *Proceedings of the Aristotelian Society*, 108(3), 289-317. Oxford, UK: Oxford University Press. 10.1111/j.1467-9264.2008.00247.x

Bloedel, J. R., & Bracha, V. (1997). Duality of cerebellar motor and cognitive functions. *International review of neurobiology*, *41*, 613-634.

Bond, K. M., & Taylor, J. A. (2015). Flexible explicit but rigid implicit learning in a visuomotor adaptation task. *Journal of Neurophysiology*, jn.00009.2015–50. http://doi.org/10.1152/jn.00009.2015

Boot, W. R., Simons, D. J., Stothart, C., and Stutts, C. (2013). The pervasive problem with placebos in psychology: why active control groups are not sufficient to rule out placebo effects. *Perspect. Psychol. Sci. 8*, 445–454. doi: 10. 1177/1745691613491271

Botvinick, M. M., Braver, T. S., Barch, D. M., Carter, C. S., & Cohen, J. D. (2001). *Conflict monitoring and cognitive control. Psychological review, 108*(3), 624.

Boucard, G. K., Albinet, C. T., Bugaiska, A., Bouquet, C. A., Clarys, D., & Audiffren, M. (2012). Impact of physical activity on executive functions in aging: a selective effect on inhibition among old adults. *Journal of Sport and Exercise Psychology*, *34*(6), 808-827.

Braver, T. S., & Barch, D. M. (2002). A theory of cognitive control, aging cognition, and neuromodulation. *Neuroscience & Biobehavioral Reviews, 26*(7), 809-817.

Buckles, V. D. (1993). Age-Related Slowing. In G. E. Stelmach & V. Hömberg (Eds.), *Sensorimotor Impairment in the Elderly* (pp. 73–87). Dordrecht: Springer Netherlands.

Buckner, R. L., Head, D., & Lustig, C. (2006). Brain changes in aging: A lifespan perspective. In E. Bialystok & F. I. M. Craik (Eds.), *Lifespan cognition: Mechanisms of change* (pp.27-42). New York: Oxford University Press.

Burch, D. (2014). What could computerized brain training learn from evidence-based medicine?. *PLoS Med*, *11*(11), e1001758.

Burke, S. N., & Barnes, C. A. (2006). Neural plasticity in the ageing brain. *Nature Reviews Neuroscience*, *7*(1), 30-40.

Burton, A. W. (1987). The effect of number of movement components on response time in children. *Journal of Human Movement Studies*, *13*, 231–247.

Busse, A. L. , Gil, G., Santarem, J. M. , and Filho, W. J. (2009). Physical activity and cognition in the elderly: a review. *Dementia e Neuropsychologia*, *3*(3), 204-208.

Butcher, P. A., Ivry, R., Kuo, S. H., Rydz, D., Krakauer, J. W., & Taylor, J. A. (2017). The Cerebellum Does More Than Sensory-Prediction-Error-Based Learning In Sensorimotor Adaptation Tasks. *Journal of Neurophysiology,118*(3), 1622-1636 http://doi.org/*10.1152/jn.00451.2017*

Cabeza, R. Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychol. Aging 17*, 85-100 (2002).

Cabeza, R., Daselaar, S. M., Dolcos, F., Prince, S. E., Budde, M., & Nyberg, L. (2004). Task-independent and task-specific age effects on brain activity during working memory, visual attention and episodic retrieval. *Cerebral cortex, 14*(4), 364-375.

Carp, J., Park, J., Hebrank, A., Park, D. C., & Polk, T. A. (2011). Age-related neural dedifferentiation in the motor system. *PLoS ONE, 6*(12), e29411.

Carroll, T. J., Lee, M., Hsu, M., and Sayde, J. (2008). Unilateral practice of a ballistic movement causes bilateral increases in performance and corticospinal excitability. *J Appl Physiol 104*, 1656–1664.

Carruthers, P. (2013). Evolution of working memory. *Proc Natl Acad Sci*, *110*(Suppl 2):10371–8. doi:10.1073/pnas.1301195110

Carson, N., Leach, L., & Murphy, K. J. (2017). A re-examination of Montreal Cognitive Assessment (MoCA) cutoff scores. *International Journal of Geriatric Psychiatry, 18*, 336–10. http://doi.org/10.1002/gps.4756

Carson, R. G., & Riek, S. (2001). Changes in muscle recruitment patterns during skill acquisition. *Experimental Brain Research*, *138*(1).

Carson, R.G. (2017). Grip strength, frailty and cognitive decline. Manuscript submitted for publication.

Cham, R., Perera, S., Studenski, S. A., & Bohnen, N. I. (2007). Striatal dopamine denervation and sensory integration for balance in middle-aged and older adults. *Gait & posture, 26*(4), 516-525.

Cham, R., Studenski, S. A., Perera, S., & Bohnen, N. I. (2008). Striatal dopaminergic denervation and gait in healthy adults. *Experimental brain research*, *185*(3), 391-398.

Chao, L. L., & Knight, R. T. (1997). Prefrontal deficits in attention and inhibitory control with aging. *Cerebral Cortex, 7*(1), 63-69.

Churchland, P., & Sejnowski, T.J. (1994). *The Computational Brain*. MIT Press

Cisek, P. (2007). Cortical mechanisms of action selection: the affordance competition hypothesis. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *362*(1485), 1585-1599.

Cisek, P., & Kalaska, J. F. (2005). Neural correlates of reaching decisions in dorsal premotor cortex: specification of multiple direction choices and final selection of action. *Neuron, 45*(5), 801-814.

Cisek, P., & Kalaska, J. F. (2010). Neural Mechanisms for Interacting with a World Full of Action Choices. *Annual Review of Neuroscience, 33*, 269--298.

Cohen, J. (1988). Statistical power analyses for the social sciences. *Hillsdale, NJ, Lawrence Erlbauni Associates*.

Cokayne, K. (2003). *Experiencing old age in ancient Rome*. New York, NY: Routledge.

Colcombe, S., & Kramer, A. F. (2003). Fitness effects on the cognitive function of older adults a meta-analytic study. *Psychological science*, *14*(2), 125-130.

Colquitt, J. A., LePine, J. A., & Noe, R. A. (2000). Toward an integrative theory of training motivation: a meta-analytic path analysis of 20 years of research. *Journal of Applied Psychology, 85*(5), 678-707. http://dx.doi.org/10.1037/0021-9010.85.5.678

Contreras-Vidal, J. L., Teulings, H., & Stelmach, G. (1998). Elderly subjects are impaired in spatial coordination in fine motor control. *Acta Psychologica, 100*(1), 25-35.

Cotman, C. W., & Berchtold, N. C. (2002). Exercise: a behavioral intervention to enhance brain health and plasticity. *Trends in neurosciences*, *25*(6), 295-301.

Courchesne, E., Chisum, H.J., Townsend, J., Cowles, A., Covington, J., Egaas, B., et al., (2000). Normal brain development and aging: quantitative analysis at in vivo MR imaging in healthy volunteers. *Radiology, 216* (3), 672--682.

Cragg, L., & Nation, K. (2008). Go or no-go? Developmental improvements in the efficiency of response inhibition in mid-childhood. *Developmental Science*, *11*(6), 819-827.

Cremen, I. A., & Carson, R. G. (2017). Have Standard Tests of Cognitive Function Been Misappropriated in the Study of Cognitive Enhancement?. *Frontiers in human neuroscience*, *11*.

Cronin, H., O'Regan, C., Finucane, C., Kearney, P., & Kenny, R. A. (2013). Health and Aging: Development of The Irish Longitudinal Study on Ageing Health Assessment. *Journal of the American Geriatrics Society, 61*(s2), S269–S278. http://doi.org/10.1111/jgs.12197

Darling, W. G., Cooke, J. D., & Brown, S. H. (1989). Control of simple arm movements in elderly humans. *Neurobiology of Aging*, *10*, 149- 157.

Davis, P. J. M., & Wright, E. A. (1977). A new method for measuring cranial cavity volume and its application to the assessment of cerebral atrophy at autopsy. *Neuropathology and applied neurobiology, 3*(5), 341-358.

Davis, S. W., Dennis, N. A., Daselaar, S. M., Fleck, M. S. & Cabeza, R. (2008). Que PASA? The posterior-anterior shift in aging. *Cereb. Cortex,18*, 1201-1209

de Chastelaine, M., Wang, T. H., Minton, B., Muftuler, L. T. & Rugg, M. D. (2011). The effects of age, memory performance, and callosal integrity on the neural correlates of successful associative encoding. *Cereb. Cortex, 21*, 2166—2176.

de Fockert, J. W., Rees, G., Frith, C. D., & Lavie, N. (2001). The role of working memory in visual selective attention. *Science*, *291*(5509), 1803-1806.

de Rugy, A., Hinder, M. R., Woolley, D. G., & Carson, R. G. (2009). The synergistic organization of muscle recruitment constrains visuomotor adaptation. *Journal of neurophysiology*, *101*(5), 2263-2269.

Deary, I. J., Corley, J., Gow, A. J., Harris, S. E., Houlihan, L. M., Marioni, R. E., et al. (2009). Age-associated cognitive decline. *British Medical Bulletin, 92*(1), 135–152. http://doi.org/10.1093/bmb/ldp033

Di Rosa, E., Hannigan, C., Brennan, S., Reilly, R., Rapčan, V., & Robertson, I. H. (2014). Reliability and validity of the Automatic Cognitive Assessment Delivery (ACAD). *Frontiers in aging neuroscience*, *6*.

Diamond, A. (2013). Executive functions. *Annual review of psychology*, *64*, 135.

Diamond, A., & Ling, D. S. (2016). Conclusions about interventions, programs, and approaches for improving executive functions that appear justified and those that, despite much hype, do not. *Accident Analysis and Prevention*, *18*, 34–48. http://doi.org/10.1016/j.dcn.2015.11.005

Donoghue, O. A., Horgan, N. F., Savva, G. M., Cronin, H., O'regan, C., & Kenny, R. A. (2012). Association between timed Up-and-Go and memory, executive function, and processing speed. *Journal of the American Geriatrics Society*, *60*(9), 1681-1686.

Duan, H., Wearne, S. L., Rocher, A. B., Macedo, A., Morrison, J. H., & Hof, P. R. (2003). Age-related dendritic and spine changes in corticocortically projecting neurons in macaque monkeys. *Cerebral Cortex, 13*(9), 950-961.

Duckworth, A. L., & Seligman, M. E. (2005). Self-discipline outdoes IQ in predicting academic performance of adolescents. *Psychological science*, *16*(12), 939-944.

Ehrler W., Huth M. (2000). "Körperliche Leistungsfähigkeit 43- bis 45-Jähriger und 62- bis 64-Jähriger im Vergleich [A comparison of the motor performance of 43–45 and 62-64 year olds]," in *Aspekte der Entwicklung im mittleren und höheren Lebensalter,* eds Martin P., Ettrich K. U., Lehr U., Roether D., Fischer-Cyrulies A., editors. (Darmstadt: Steinkopff;), 220–234

Engel, A. K., Maye, A., Kurthen, M., & König, P. (2013). Where's the action? The pragmatic turn in cognitive science. *Trends in Cognitive Sciences*, *17*(5), 202–209. http://doi.org/10.1016/j.tics.2013.03.006

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. *Perception & psychophysics*, *16*(1), 143-149.

Etnier, J. L., Nowell, P. M., Landers, D. M., & Sibley, B. A. (2006). A meta-regression to examine the relationship between aerobic fitness and cognitive performance. *Brain research reviews*, *52*(1), 119-130.

Etnier, J. L., Nowell, P. M., Landers, D. M., & Sibley, B. A. (2006). A meta-regression to examine the relationship between aerobic fitness and cognitive performance. *Brain Research Reviews*, *52*(1), 119–130. http://doi.org/10.1016/j.brainresrev.2006.01.002

Etnier, J. L., Salazar, W., Landers, D. M., Petruzzello, S. J., Han, M., & Nowell, P. (1997). The influence of physical fitness and exercise upon cognitive functioning: a meta-analysis. *Journal of sport and Exercise Psychology*, *19*(3), 249-277.

Fitts, P. M. (1954). The information capacity of the human motor system in controlling the amplitude of movement. *Journal of experimental psychology*, *47*(6), 381.

Fjell, A. M., & Walhovd, K. B. (2010). Structural brain changes in aging: courses, causes and cognitive consequences. *Reviews in the Neurosciences*, *21*(3), 187-222.

Flament, D., Ellermann, J. M., Kim, S. G., Uğurbil, K., & Ebner, T. J. (1996). Functional magnetic resonance imaging of cerebellar activation during the learning of a visuomotor dissociation task. *Human brain mapping*, *4*(3), 210-226.

Flanagan, J. R., & Johansson, R. S. (2003). Action plans used in action observation. *Nature*, *424*(6950), 769-771.

Fodor, J.A. (1981). *Representations: Essays on the Foundations of Cognitive Science*. MIT Press.

Forte, R., Boreham, C. A., Leite, J. C., De Vito, G., Brennan, L., Gibney, E. R., & Pesce, C. (2013). Enhancing cognitive functioning in the elderly: multicomponent vs resistance training. *Clinical interventions in aging*, 8.

Ge, Y., Grossman, R. I., Babb, J. S., Rabin, M. L., Mannon, L. J., & Kolson, D. L. (2002). Age-related total gray matter and white matter changes in normal adult brain. Part I: volumetric MR imaging analysis. *American journal of neuroradiology*, *23*(8), 1327-1333.

Gelman, A., & Rubin, D. B. (1992). Inference from iterative simulation using multiple sequences. *Statistical science*, 457-472.

Georgopoulos, A.P., Massey, J.T., (1987). Cognitive spatial–motor processes. 1. The making of movements at various angles from a stimulus direction. *Exp. Brain Res. 65*, 361–370.

Gibson, J. J. (1966). *The senses considered as perceptual systems*. Boston: Houghton - Mifflin.

Glicksohn, J., & Kinberg, Z. (2009). Performance on embedded figures tests: profiling individual differences. *Journal of Individual Differences*, *30*(3), 152-162.

Glisky, E.L. (2007). Changes in cognitive function in human aging. In D.R. Riddle, (Ed.). (2007). *Brain aging: Models, methods, mechanisms* (pp. 3-20). Boca Raton, FL: CRC Press

Gold, J. I., & Shadlen, M. N. (2007). The neural basis of decision-making. *Annu. Rev. Neurosci., 30*, 535-574.

Goldberg, T. E., Harvey, P. D., Wesnes, K. A., Snyder, P. J., & Schneider, L. S. (2015). Practice effects due to serial cognitive assessment: Implications for preclinical Alzheimer's disease randomized controlled trials. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *1*(1), 103-111.

Good, C.D., Johnsrude, I.S., Ashburner, J., Henson, R.N., Friston, K.J., Frackowiak, R.S., (2001). A voxel-based morphometric study of ageing in 465 normal adult human brains. *Neuroimage 14* (1 Pt 1), 21--36.

Gotham, A. M., Brown, R.G., Marsden, C. D. (1988). "Frontal" cognitive function in patients with Parkinson's disease "on" and "off" levodopa. *Brain 111*:299–321

Gothe, N., Pontifex, M. B., Hillman, C., & McAuley, E. (2013). The acute effects of yoga on executive function. *Journal of Physical Activity & Health*, *10*(4), 488–495.

Gottfries, C. G. (1990). Neurochemical aspects on aging and diseases with cognitive impairment. *Journal of neuroscience research, 27*(4), 541-547.

Gottwald, J. M., Achermann, S., Marciszko, C., Lindskog, M., & Gredebäck, G. (2016). An embodied account of early executive functions development: Prospective motor control in infancy is related to prohibition and working memory. *Psychological Science*, *27*.

Grady, C. (2012). The cognitive neuroscience of ageing. *Nature Reviews Neuroscience, 13*(7), 491-505.

Grady, C. L., McIntosh, A. R., Bookstein, F., Horwitz, B., Rapoport, S. I., & Haxby, J. V. (1998). Age-related changes in regional cerebral blood flow during working memory for faces. *Neuroimage*, *8*(4), 409-425.

Gunning-Dixon, F. M., Head, D., McQuain, J., Acker, J. D., & Raz, N. (1998). Differential aging of the human striatum: a prospective MR imaging study. *American Journal of Neuroradiology*, *19*(8), 1501-1507.

Gurney, K., Prescott, T. J., & Redgrave, P. (2001). A computational model of action selection in the basal ganglia. I. A new functional anatomy. *Biological cybernetics*, *84*(6), 401-410.

Gutchess, A. (2014). Plasticity of the aging brain: new directions in cognitive neuroscience. *Science, 346*(6209), 579–582. http://doi.org/10.1126/science.1254604

Guye, S., & Bastian, von, C. C. (2017). Working Memory Training in Older Adults: Bayesian Evidence Supporting the Absence of Transfer. *Psychology and Aging* (pp. 1–47).

Haaland, K. Y., Vranes, L. F., Goodwin, J. S., & Garry, P. J. (1987). Wisconsin Card Sort Test performance in a healthy elderly population. *Journal of Gerontology*, *42*(3), 345-346.

Hadfield, J. D. (2010). MCMC methods for multi-response generalized linear mixed models: the MCMCglmm R package. *Journal of Statistical Software*, *33*(2), 1-22.

Hamacher, D., Herold, F., Wiegel, P., Hamacher, D., and Schega, L. (2015). Brain activity during walking: a systematic review. *Neurosci. Biobehav. Rev. 57*, 310–327. doi: 10.1016/j.neubiorev.2015.08.002

Hamra, G., MacLehose, R., & Richardson, D. (2013). Markov chain Monte Carlo: An introduction for epidemiologists. *International Journal of Epidemiology, 42,* 627–634. http://dx.doi.org/10.1093/ije/dyt043

Hanks, R. A., Rapport, L. J., Millis, S. R., & Deshpande, S. A. (1999). Measures of executive functioning as predictors of functional ability and social integration in a rehabilitation sample. *Archives of physical medicine and rehabilitation*, *80*(9), 1030-1037.

Hasher, L., & Zacks, R. T. (1988). Working memory, comprehension, and aging: A review and a new view. *Psychology of learning and motivation*, *22*, 193-225.

Haug, H., & Eggers, R. (1991). Morphometry of the human cortex cerebri and corpus striatum during aging. *Neurobiology of aging, 12*(4), 336-338.

Head, D., Kennedy, K. M., Rodrigue, K. M., & Raz, N. (2009). Age differences in perseveration: cognitive and neuroanatomical mediators of performance on the Wisconsin Card Sorting Test. *Neuropsychologia, 47*(4), 1200-1203.

Hellebrandt, F. A. (1951). Cross education; ipsilateral and contralateral effects of unimanual training. *J Appl Physiol 4*, 136–144.

Hertzog, C., Kramer, A. F., Wilson, R. S,. & Lindenberger, U. (2008). Enrichment effects on adult cognitive development: can the functional capacity of older adults be preserved and enhanced? *Psychological Science in the Public Interest, 9*(1): 1–65.

Heuninckx, S., Wenderoth, N., & Swinnen, S. P. (2008). Systems neuroplasticity in the aging brain: recruiting additional neural resources for successful motor performance in elderly persons. *The Journal of Neuroscience: the Official Journal of the Society for Neuroscience, 28*(1), 91--99.

Heuninckx, S., Wenderoth, N., Debaere, F., Peeters, R., & Swinnen, S. P. (2005). Neural basis of aging: the penetration of cognition into action control. *The Journal of Neuroscience: the Official Journal of the Society for Neuroscience, 25*(29), 6787--6796.

Hillman, C. H., Buck, S. M., Themanson, J. R., Pontifex, M. B., & Castelli, D. M. (2009). Aerobic fitness and cognitive development: Event-related brain potential and task performance indices of executive control in preadolescent children. *Developmental psychology, 45*(1), 114.

Hinder, M. R., Fujiyama, H., & Summers, J. J. (2012). Premotor-motor interhemispheric inhibition is released during movement initiation in older but not young adults. *PloS one, 7*(12), e52573.

Hinder, M. R., Riek, S., Tresilian, J. R., de Rugy, A., & Carson, R. G. (2010). Real-time error detection but not error correction drives automatic visuomotor adaptation. *Experimental Brain Research*, *201*(2), 191–207. http://doi.org/10.1007/s00221-009-2025-9

Hinder, M. R., Schmidt, M. W., Garry, M. I., Carroll, T. J., and Summers, J. J. (2011). Absence of cross-limb transfer of performance gains following ballistic motor practice in older adults. *J Appl Physiol* 110, 166–175.

Hinder, M. R., Tresilian, J. R., Riek, S., & Carson, R. G. (2008). The contribution of visual feedback to visuomotor adaptation: How much and when? *Brain Research*, *1197*, 123–134. http://doi.org/10.1016/j.brainres.2007.12.067

Holtzer, R., Verghese, J., Xue, X., & Lipton, R. B. (2006). Cognitive processes related to gait velocity: results from the Einstein Aging Study. *Neuropsychology*, *20*(2), 215.

Holtzer, R., Wang, C., Verghese, J. (2012). The relationship between attention and gait in aging: facts and fallacies. *Motor Control, 16*(1):64--80.

Hommel, B. (2011). Attention and spatial stimulus coding in the Simon task: a rejoinder to van der Lubbe and Abrahamse (2010). *Acta psychologica*, *136*(2), 265-268.

Hommel, B., Li, K. Z., & Li, S. C. (2004). Visual search across the life span. *Developmental psychology*, *40*(4), 545.

Horn, J. L. (Ed.). (1986). *Intellectual stability concepts.* Hillsdale: Erblaum.

Houk, J. C., Bastianen, C., Fansler, D., Fishbach, A., Fraser, D., Reber, P. J., ... & Simo, L. S. (2007). Action selection and refinement in subcortical loops through basal ganglia and cerebellum. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *362*(1485), 1573-1583.

Hubert, M., & Vandervieren, E. (2008). An adjusted boxplot for skewed distributions. *Computational statistics & data analysis, 52*(12), 5186-5201.

Ince, P. (2001). Pathological correlates of late-onset dementia in a multicenter community-based population in England and Wales. *Lancet, 357:* 169–175.

Isoda, M., & Hikosaka, O. (2011). Cortico-basal ganglia mechanisms for overcoming innate, habitual and motivational behaviors. *European Journal of Neuroscience*, *33*(11), 2058-2069.

Ito, M. (1993). Movement and thought: identical control mechanisms by the cerebellum. *Trends Neurosci*., *16*(11):448–50.

Jaeggi, S. M., Buschkuehl, M., Etienne, A., Ozdoba, C., Perrig, W. J., & Nirkko, A. C. (2007). On how high performers keep cool brains in situations of cognitive overload. *Cognitive, Affective, and Behavioral Neuroscience, 7*(2), 75 89.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences*, *105*(19), 6829-6833.

Jaeggi, S. M., Schmid, C., Buschkuehl, M., & Perrig, W. J. (2009). Differential age effects in load-dependent memory processing. *Aging, Neuropsychology, and Cognition, 16*, 80 102.

Jaeggi, S. M., Seewer, R., Nirkko, A. C., Eckstein, D., Schroth, G., Groner, R., & Gutbrod, K. (2003). Does excessive memory load attenuate activation in the prefrontal cortex? Load-dependent processing in single and dual tasks: functional magnetic resonance imaging study. *NeuroImage, 19*(2), 210-225.

Jansen, P., Titze, C., & Heil, M. (2009). The influence of juggling on mental rotation performance. *International Journal of Sport Psychology, 40*, 351–359.

Jernigan, T.L., Archibald, S.L., Fennema-Notestine, C., Gamst, A.C., Stout, J.C., Bonner, J., Hesselink, J.R., (2001). Effects of age on tissues and regions of the cerebrum and cerebellum. *Neurobiol. Aging 22*, 581--594,

Jobe, J. B., Smith, D. M., Ball, K., Tennstedt, S. L., Marsiske, M., Willis, S. L., ... & Kleinman, K. (2001). ACTIVE: A cognitive intervention trial to promote independence in older adults. *Controlled clinical trials*, *22*(4), 453-479.

Johann, V. E., Stenger, K., Kersten, S., & Karbach, J. (2016). Effects of motor-cognitive coordination training and cardiovascular training on motor coordination and cognitive functions. *Psychology of Sport & Exercise*, 24(C), 118-127. doi: 10.1016/j.psychsport.2016.01.008

Jonides, J. (2004). How does practice makes perfect? *Nat. Neurosci.* 7, 10–11. doi: 10.1038/nn0104-10

Kaasinen, V., & Rinne, J. O. (2002). Functional imaging studies of dopamine system and cognition in normal aging and Parkinson's disease. *Neuroscience & Biobehavioral Reviews, 26*(7), 785-793.

Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M., Turner, R., et al. (1998). The acquisition of skilled motor performance: fast and slow experience-driven changes in primary motor cortex. *Proc Natl Acad Sci U S A, 95*(3), 861-868.

Katzman, R., Aronson, M., Fuld, P., Kawas, C., Brown, T., Morgenstern, H., Frishman, W., Gidez, L., Eder, H., & Ooi, W.L. (1989). Development of dementing illnesses in an 80-year-old volunteer cohort. *Annals of Neurology, 25*, 317–324.

Kennedy, G., Hardman, R. J., Macpherson, H., Scholey, A. B., & Pipingas, A. (2016). How Does Exercise Reduce the Rate of Age-Associated Cognitive Decline? A Review of Potential Mechanisms. *Journal of Alzheimer's Disease, 55*(1), 1–18. http://doi.org/10.3233/JAD-160665.

Ketcham, C. J., Stelmach, G. E., Birren, J., & Schaie, K. W. (2001). Age-related declines in motor control. *Handbook of the psychology of aging*, *5*, 313-348.

Kongs, S. K., Thompson, L. L., Iverson, G. L., & Heaton, R. K. (2000). Wisconsin card sorting test-64 card version (WCST-64). *Odessa, FL: Psychological Assessment Resources*.

Koziol, L. F., Budding, D. E., & Chidekel, D. (2011). From Movement to Thought: Executive Function, Embodied Cognition, and the Cerebellum. *The Cerebellum, 11*(2), 505–525. http://doi.org/10.1007/s12311-011-0321-y

Koziol, L. F., Budding, D., Andreasen, N., D'Arrigo, S., Bulgheroni, S., Imamizu, H., ... & Pezzulo, G. (2014). Consensus paper: the cerebellum's role in movement and cognition. *The Cerebellum, 13*(1), 151-177.

Kramer, A. F., Bherer, L., Colcombe, S. J., Dong, W., & Greenough, W. T. (2004). Environmental influences on cognitive and brain plasticity during aging. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 59*(9), M940-M957.

Kramer, A. F., Erickson, K. I., Colcombe, S. J. (2006). Exercise, cognition, and the aging brain. *J Appl Physiol, 101*:1237-1242.

Kramer, J. H., Mungas, D., Reed, B. R., Wetzel, M. E., Burnett, M. M., Miller, B. L., ... & Chui, H. C. (2007). Longitudinal MRI and cognitive change in healthy elderly. *Neuropsychology*, *21*(4), 412.

Kruschke, J. (2014). *Doing Bayesian data analysis: A tutorial with R, JAGS, and Stan*. Academic Press.

Kruschke, J. K. (2010). Bayesian data analysis. *Wiley Interdisciplinary Reviews: Cognitive Science*, *1*(5), 658-676.

Kruschke, J. K. (2013). Bayesian estimation supersedes the t test. *Journal of Experimental Psychology: General*, *142*(2), 573–603. http://doi.org/10.1037/a0029146

Kruschke, J. K., & Liddell, T. M. (2017). The Bayesian New Statistics: Hypothesis testing, estimation, meta-analysis, and power analysis from a Bayesian perspective. *Psychonomic Bulletin & Review*, 1-29.

Kueider, A. M., Parisi, J. M., Gross, A. L., Rebok, G. W. (2012). Computerized Cognitive Training with Older Adults: A Systematic Review. *PLoS ONE 7*(7)

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. *PLoS Med,* 1*1*(11), e1001756.

Larish, D. D., & Stelmach, G. E. (1982). Preprogramming, programming, and reprogramming of aimed hand movements as a function of age. *Journal of Motor Behavior*, *14*(4), 322-340.

Lauenroth, A., Ioannidis, A. E., & Teichmann, B. (2016). Influence of combined physical and cognitive training on cognition: a systematic review. *BMC geriatrics*, *16*(1), 141.

Lay, B. S., Sparrow, W. A., Hughes, K. M., & O'Dwyer, N. J. (2002). Practice effects on coordination and control, metabolic energy expenditure, and muscle activation. *Human movement science*, *21*(5), 807-830.

Lee, M., Hinder, M. R., Gandevia, S. C., and Carroll, T. J. (2010). The ipsilateral motor cortex contributes to cross-limb transfer of performance gains after ballistic motor practice. *J Physiol 588*, 201–212.

Lees AJ, Smith E (1983) Cognitive deficits in the early stages of Parkinson's disease. *Brain 106*:257–270.

Lenth, R. V., & Hervé, M. (2015). lsmeans: Least-squares means. *R package version*, *2*, 20-3.

Levin, O., Fujiyama, H., Boisgontier, M. P., Swinnen, S. P., & Summers, J. J. (2014). Aging and motor inhibition: a converging perspective provided by brain

stimulation and imaging approaches. *Neuroscience & Biobehavioral Reviews,43*, 100-117.

Lezak, M. D. (2004). *Neuropsychological assessment*. Oxford University Press, USA.

Li, S. C., Lindenberger, U., & Sikström, S. (2001). Aging cognition: from neuromodulation to representation. *Trends in cognitive sciences, 5(*11), 479-486.

Lindsay, J., Laurin, D., Verreault, R., Hébert, R., Helliwell, B., Hill, G. B., & McDowell, I. (2002). Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging. *American journal of epidemiology, 156*(5), 445-453.

Lutz, H. (2012). Life Kinetik® - Gehirntraining durch Bewegung (3. Aufl.). München: Bayrischer Landwitschaftsverlag.

Manganotti, P., Gerloff, C., Toro, C., Katsuta, H., Sadato, N., Zhuang, P. A., ... & Hallett, M. (1998). Task-related coherence and task-related spectral power changes during sequential finger movements. *Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control*, *109*(1), 50-62.

Manly, T., Robertson, I. H., Galloway, M., & Hawkins, K. (1999). The absent mind: further investigations of sustained attention to response. *Neuropsychologia*, *37*(6), 661-670.

Mattay, V. S., Fera, F., Tessitore, A., Hariri, A. R., Das, S., Callicott, J. H., & Weinberger, D. R. (2002). Neurophysiological correlates of age-related changes in human motor function. *Neurology, 58*(4), 630-635.

McDougle, S. D., Bond, K. M., & Taylor, J. A. (2015). Explicit and Implicit Processes Constitute the Fast and Slow Processes of Sensorimotor Learning. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*, *35*(26), 9568–9579. http://doi.org/10.1523/JNEUROSCI.5061-14.2015

McDougle, S. D., Ivry, R. B., & Taylor, J. A. (2016). Taking aim at the cognitive side of learning in sensorimotor adaptation tasks. *Trends in cognitive sciences*, *20*(7), 535-544.

McGann, M. (2007) Enactive theorists do it on purpose: toward an enactive account of goals and goal-directedness *Phenom. Cogn. Sci. 6*, 463–483.

Melby-Lervåg, M., & Hulme, C. (2013). Is working memory training effective? A meta-analytic review. *Developmental psychology*, *49*(2), 270.

Melby-Lervåg, M., Redick, T. S., & Hulme, C. (2016). Working Memory Training Does Not Improve Performance on Measures of Intelligence or Other Measures of "Far Transfer" Evidence From a Meta-Analytic Review. *Perspectives on Psychological Science*, *11*(4), 512-534.

Mendoza, G., & Merchant, H. (2014). Motor system evolution and the emergence of high cognitive functions. *Progress in Neurobiology*, *122*, 73–93. http://doi.org/10.1016/j.pneurobio.2014.09.001

Merabet, L. B., Hamilton, R., Schlaug, G., Swisher, J. D., Kiriakopoulos, E. T., Pitskel, N. B., ... & Pascual-Leone, A. (2008). Rapid and reversible recruitment of early visual cortex for touch. *PLoS One*, *3*(8), e3046.

Miller, R. (2007). *A theory of the basal ganglia and their disorders.* Boca Raton: CRC Press.

Milner B (1963) Effects of brain lesions on card sorting. *Arch Neurol 9*:90–100.

Mirelman, A., Weiss, A., Buchman, A. S., Bennett, D. A., Giladi, N., & Hausdorff, J. M. (2014). Association Between Performance on Timed Up and Go Subtasks and Mild Cognitive Impairment: Further Insights into the Links Between Cognitive and Motor Function. *Journal of the American Geriatrics Society, 62*(4), 673--678.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive psychology, 41*(1), 49-100.

Moffitt, T. E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R. J., Harrington, H., ... & Sears, M. R. (2011). A gradient of childhood self-control predicts health, wealth, and public safety. *Proceedings of the National Academy of Sciences*, *108*(7), 2693-2698.

Morcom, A. M., Li, J., & Rugg, M. D. (2007). Age effects on the neural correlates of episodic retrieval: increased cortical recruitment with matched performance. *Cerebral Cortex, 17*(11), 2491--2506.

Moreau, D. (2012). The role of motor processes in three-dimensional mental rotation: Shaping cognitive processing via sensorimotor experience. *Learning and Individual Differences*, *22*(3), 354–359.

Moreau, D. (2015). Unreflective actions? complex motor skill acquisition to enhance spatial cognition. *Phenomenology and the Cognitive Sciences, 14*(2), 349–359. http://doi.org/10.1007/s11097-014-9376-9

Moreau, D. and Conway, A.R.A. (2013). Cognitive enhancement: a comparative review of computerized and athletic training programs. *Int. Rev. Sport Exerc. Psychol. 6,* 155–183

Moreau, D., & Conway, A. R. A. (2014). The case for an ecological approach to cognitive training. *Trends in Cognitive Sciences*, *18*(7), 334–336. http://doi.org/10.1016/j.tics.2014.03.009

Moreau, D., Kirk, I. J., & Waldie, K. E. (2016). Seven Pervasive Statistical Flaws in Cognitive Training Interventions. *Frontiers in Human Neuroscience*, *10*, 35. http://doi.org/10.3389/fnhum.2016.00153

Moreau, D., Morrison, A. B., & Conway, A. R. (2015). An ecological approach to cognitive enhancement: Complex motor training. *Acta psychologica*, *157*, 44-55.

Morrison, A. B., & Chein, J. M. (2011). Does working memory training work? The promise and challenges of enhancing cognition by training working memory. *Psychonomic bulletin & review*, *18*(1), 46-60.

Morrison, J. H., & Baxter, M. G. (2012). The ageing cortical synapse: hallmarks and implications for cognitive decline. *Nature Reviews Neuroscience, 13*(4), 240-250.

Mueller, S. T., & Piper, B. J. (2014). The psychology experiment building language (PEBL) and PEBL test battery. *Journal of neuroscience methods*, *222*, 250-259.

Mukhopadhyay, P., Dutt, A., Kumar Das, S., Basu, A., Hazra, A., Dhibar, T., & Roy, T. (2007). Identification of neuroanatomical substrates of set-shifting ability: evidence from patients with focal brain lesions. *Progress in Brain Research, 168*, 95-104.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., ... & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), 695-699.

Nelson, H. E. (1976). A modified card sorting test sensitive to frontal lobe defects. *Cortex*, *12*(4), 313-324.

Neubert, F. X., Mars, R. B., & Rushworth, M. F. (2013). Is there an inferior frontal cortical network for cognitive control and inhibition. *Principles of frontal lobe function,* Ed, 2, 332-352.

Newkirk, L. A., Kim, J. M., Thompson, J. M., Tinklenberg, J. R., Yesavage, J. A., & Taylor, J. L. (2004). Validation of a 26-Point Telephone Version of the Mini-Mental State Examination. *Journal of Geriatric Psychiatry and Neurology*, *17*(2), 81–87. http://doi.org/10.1177/0891988704264534

Niemann, C., Godde, B., & Voelcker-Rehage, C. (2014). Not only cardiovascular, but also coordinative exercise increases hippocampal volume in older adults. *Frontiers in aging neuroscience, 6*.

Niemann, C., Godde, B., & Voelcker-Rehage, C. (2016). Senior Dance Experience, Cognitive Performance, and Brain Volume in Older Women. *Neural Plasticity*, *2016*(3), 1–10. http://doi.org/10.1155/2016/9837321

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective, & Behavioral Neuroscience*, *12*(2), 241-268.

Northey, J. M., Cherbuin, N., Pumpa, K. L., Smee, D. J., & Rattray, B. (2017). Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med*, bjsports-2016.

Nouchi, R., Taki, Y., Takeuchi, H., Hashizume, H., Shigemune, Y., Akitsuki, Y., et al. (2012). Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial. *PLoS ONE 7*.

Nyberg, L., Lövdén, M., Riklund, K., Lindenberger, U. & Bäckman, L. (2012). Memory aging and brain maintenance. Trends Cogn. *Sci. 16*, 292–305.

Nyhus, E., & Barceló, F. (2009). The Wisconsin Card Sorting Test and the cognitive assessment of prefrontal executive functions: A critical update. *Brain and Cognition*, *71*(3), 437–451.

O'Regan, J. K., & Noë, A. (2001). A sensorimotor account of vision and visual consciousness. *The Behavioral and Brain Sciences, 24*(5), 939–73–discussion 973–1031. http://doi.org/10.1017/S0140525X01000115

Ohbayashi, M., Ohki, K., & Miyashita, Y. (2003). Conversion of working memory to motor sequence in the monkey premotor cortex. *Science, 301*(5630), 233-236.

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, *9*(1), 97-113.

Oswald, W. D., Gunzelmann, T., Rupprecht, R., Hagen, B. (2006). Differential effects of single versus combined cognitive and physical training with older adults: the SimA study in a 5-year perspective. *Eur J Ageing*, *3*(4):179–192.

Owen, A. M., Hampshire, A., Grahn, J. A., Stenton, R., Dajani, S., Burns, A. S., ... & Ballard, C. G. (2010). Putting brain training to the test. *Nature*, *465*(7299), 775-778.

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human brain mapping, 25*(1), 46-59.

Paoletti, P. (2008). *Crescere nell'eccellenza.* Rome: Armando Publishing.

Papp, K. V., Walsh, S. J., & Snyder, P. J. (2009). Immediate and delayed effects of cognitive interventions in healthy elderly: A review of current literature and future directions. *Alzheimer's & Dementia, 5*(1), 50-60.

Park, D. C. et al. Models of visuospatial and verbal memory across the adult life span. *Psychol. Aging 17*, 299–320 (2002).

Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual review of psychology, 60*, 173.

Park, D. C., Polk, T. A., Mikels, J. A., Taylor, S. F., Marshuetz, C. M. (2001). Cerebral aging: integration of brain and behavioral models of cognitive function. *Dialogues Clin. Neurosci., 3*, 151--165.

Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proceedings of the National Academy of Sciences of the United States of America, 101*(35), 13091-13095.

Park, S., Kwon, E., & Lee, H. (2017). Life Course Trajectories of Later-Life Cognitive Functions: Does Social Engagement in Old Age Matter?. *International journal of environmental research and public health*, *14*(4), 393.

Paulesu, E., Frith, C. D., & Frackowiak, R. S. (1993). The neural correlates of the verbal component of working memory. *Nature, 362*(6418), 342-345.

Pesce, C. (2012). Shifting the focus from quantitative to qualitative exercise characteristics in exercise and cognition research. *Journal of Sport and Exercise Psychology*, *34*(6), 766-786.

Pesce, C., Crova, C., Marchetti, R., Struzzolino, I., Masci, I., Vannozzi, G., & Forte, R. (2013). Searching for cognitively optimal challenge point in physical activity

for children with typical and atypical motor development. *Mental Health and Physical Activity*, *6*(3), 172-180.

Peters, M., Laeng, B., Latham, K., Jackson, M., Zaiyouna, R., & Richardson, C. (1995). A redrawn Vandenberg and Kuse Mental Rotations Test: Different versions and factors that affect performance. *Brain and Cognition, 28*, 39–58.

Petersen, R. C., Jack, C. R., Xu, Y. C., Waring, S. C., O'brien, P. C., Smith, G. E., ... & Kokmen, E. (2000). Memory and MRI-based hippocampal volumes in aging and AD. *Neurology*, *54*(3), 581-581.

Pezzulo, G. (2011). Grounding procedural and declarative knowledge in sensorimotor anticipation. *Mind & Language*, *26*(1), 78-114.

Plamondon, R., & Alimi, A. M. (1997). Speed/accuracy trade-offs in target-directed movements. *Behavioral and brain sciences*, *20*(2), 279-303.

Plassman, B. L., Langa, K. M., Fisher, G. G., Heeringa, S. G., Weir, D. R., Ofstedal, M. B., et al. (2008). Prevalence of Cognitive Impairment without Dementia in the United States. *Annals of Internal Medicine*, 148(6), 427-W490.

Podsiadlo, D., & Richardson, S. (1991). The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of the American geriatrics Society, 39*(2), 142-148.

Purdy, M. H. (2011). Executive functions: Theory, assessment, and treatment. *Cognitive communication disorders*, 77-93.

R Core Team (2014). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: integration of structural and functional findings. In F. I. M. Craik & T. Salthouse, (Eds): *Handbook of aging and cognition II*, (pp. 1--90). Hillsdale, NJ: Erlbaum.

Raz, N., & Rodrigue, K. M. (2006). Differential aging of the brain: patterns, cognitive correlates and modifiers. *Neuroscience & Biobehavioral Reviews,30*(6), 730-748.

Raz, N., Ghisletta, P., Rodrigue, K. M., Kennedy, K. M., & Lindenberger, U. (2010). Trajectories of brain aging in middle-aged and older adults: regional and individual differences. *Neuroimage*, *51*(2), 501-511.

Raz, N., Gunning-Dixon, F., Head, D., Rodrigue, K.M., Williamson, A., Acker, J.D., (2004). Aging, sexual dimorphism, and hemispheric asymmetry of the

cerebral cortex: replicability of regional differences in volume. *Neurobiol. Aging 25* (3), 377- 396.

Raz, N., Gunning, F.M., Head, D., Dupuis, J.H., McQuain, J., Briggs, S.D., et al., (1997). Selective aging of the human cerebral cortex observed in vivo: differential vulnerability of the prefrontal gray matter. *Cereb. Cortex 7* (3), 268--282.

Raz, N., Lindenberger, U., Rodrigue, K. M., Kennedy, K. M., Head, D., Williamson, A., ... & Acker, J. D. (2005). Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cerebral cortex*, *15*(11), 1676-1689.

Redick, T. S., & Lindsey, D. R. (2013). Complex span and n-back measures of working memory: a meta-analysis. *Psychonomic bulletin & review*, *20*(6), 1102-1113.

Resnick, S. M., Pham, D. L., Kraut, M. A., Zonderman, A. B., & Davatzikos, C. (2003). Longitudinal magnetic resonance imaging studies of older adults: a shrinking brain. *The Journal of Neuroscience, 23*(8), 3295-3301.

Reuter-Lorenz, P. A., & Park, D. C. (2014). How does it STAC up? Revisiting the scaffolding theory of aging and cognition. *Neuropsychology review*, *24*(3), 355-370.

Reuter-Lorenz, P. A., Jonides, J., Smith, E. E., Hartley, A., Miller, A., Marshuetz, C., & Koeppe, R. A. (2000). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. *Journal of cognitive neuroscience, 12*(1), 174-187.

Reuter-Lorenz, P. A., Stanczak, L., Miller, A. (1999). Neural recruitment and cognitive aging: two hemispheres are better than one especially as you age. *Psychol Sci, 10*:494--500.

Reuter, E.-M., Behrens, M., & Zschorlich, V. R. (2015). Age-related differences in corticomotor facilitation indicate dedifferentiation in motor planning. Exg, *65*(C), 79--84.

Rhodes, M. G. (2004). Age-related differences in performance on the Wisconsin card sorting test: a meta-analytic review. *Psychology and Aging, 19*(3), 482-494.

Roberts, R. D., & Pallier, G. (2001). Individual differences in performance on elementary cognitive tasks (ECTs): lawful vs. problematic parameters. *J Gen Psycho, 128*, 279-314.

Robertson, D. A., Savva, G. M., & Kenny, R. A. (2013). Frailty and cognitive impairment--A review of the evidence and causal mechanisms. *Ageing Research Reviews, 12*(4), 840--851.

Robertson, I. H., Manly, T., Andrade, J., Baddeley, B. T., & Yiend, J. (1997). 'Oops!': Performance correlates of everyday attentional failures in trau- matic brain injured and normal subjects. *Neuropsychologia*, *35*(6), 747– 758.

Robinson, A. L., Heaton, R. K., Lehman, R. A., & Stilson, D. W. (1980). The utility of the Wisconsin Card Sorting Test in detecting and localizing frontal lobe lesions. *Journal of Consulting and Clinical Psychology, 48*, 605–614.

Roig, M., Nordbrandt, S., Geertsen, S. S., & Nielsen, J. B. (2013). The effects of cardiovascular exercise on human memory: a review with meta-analysis. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1645-1666.

Rönnlund, M., Nyberg, L., Bäckman, L., & Nilsson, L. G. (2005). Stability, growth, and decline in adult life span development of declarative memory: cross-sectional and longitudinal data from a population-based study. *Psychology and aging*, *20*(1), 3.

Rosano, C., Aizenstein, H., Brach, J., Longenberger, A., Studenski, S., & Newman, A. B. (2008). Special Article Gait Measures Indicate Underlying Focal Gray Matter Atrophy in the Brain of Older Adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 63*(12), 1380-1388.

Rosch, E., Thompson, L., & Varela, F. J. (1991). The embodied mind: Cognitive science and human experience.

Rosnow, R., & Rosenthal, R. (1997). *People studying people: Artifacts and ethics in behavioral research*. WH Freeman.

Ruddy, K. L., Rudolf, A. K., Kalkman, B., King, M., Daffertshofer, A., Carroll, T. J., & Carson, R. G. (2016). Neural adaptations associated with interlimb transfer in a ballistic wrist flexion task. *Frontiers in human neuroscience*, *10*.

Rypma, B., & D'Esposito, M. (2000). Isolating the neural mechanisms of age-related changes in human working memory. *Nature neuroscience, 3*(5), 509-515.

Rypma, B., & D'Esposito, M. (1999). The roles of prefrontal brain regions in components of working memory: effects of memory load and individual differences. *Proceedings of the National Academy of Sciences, 96*(11), 6558-6563.

Salat, D.H., Buckner, R.L., Snyder, A.Z., Greve, D.N., Desikan, R.S., Busa, E., Morris, J.C., Dale, A.M., Fischl, B., (2004). Thinning of the cerebral cortex in aging. *Cereb. Cortex, 14*, 721--730.

Salthouse, T. A. (1996). The processing-speed theory of adult age differences in cognition. *Psychological Review, 103*, 403--437.

Salthouse, T. A. (2000). Aging and measures of processing speed. *Biological psychology*, *54*(1), 35-54.

Salthouse, T. A., Atkinson, T. M., & Berish, D. E. (2003). Executive functioning as a potential mediator of age-related cognitive decline in normal adults. *Journal of Experimental Psychology: General, 132*(4), 566.

Sanchez-Cubillo, I., Perianez, J. A., Adrover-Roig, D., Rodriguez-Sanchez, J. M., Rios-Lago, M., Tirapu, J. E. E. A., & Barcelo, F. (2009). Construct validity of the Trail Making Test: role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. *Journal of the International Neuropsychological Society*, *15*(3), 438.

Scarmeas, N., Levy, G., Tang, M., Manly, J., Stern, Y. (2001). Influence of leisure activity on the incidence of Alzheimer's disease. *Neurology*, 57, 2236-2242.

Schmahmann, J.D. (1997). *The cerebellum and cognition.* Academic; London.

Schmidt, R. A., Zelaznik, H. N., & Frank, J. S. (1978). Sources of inaccuracy in rapid movement. *Information processing in motor control and learning*, 183-203.

Schuch, S., Bayliss, A. P., Klein, C., & Tipper, S. P. (2010). Attention modulates motor system activation during action observation: evidence for inhibitory rebound. *Experimental Brain Research*, *205*(2), 235-249.

Schween, R., & Hegele, M. (2017). Feedback delay attenuates implicit but facilitates explicit adjustments to a visuomotor rotation. *Neurobiology of learning and memory*, *140*, 124-133.

Seeley, W. W., Crawford, R. K., Zhou, J., Miller, B. L., & Greicius, M. D. (2009). Neurodegenerative diseases target large-scale human brain networks. *Neuron*, *62*(1), 42-52.

Seidler, R. D., & Carson, R. G. (2017). Sensorimotor Learning: Neurocognitive Mechanisms and Individual Differences. *Journal of neuroengineering and rehabilitation*, *14*(1), 74.

Seidler, R. D., & Noll, D. C. (2008). Neuroanatomical correlates of motor acquisition and motor transfer. *Journal of neurophysiology*, *99*(4), 1836-1845.

Seidler, R. D., & Stelmach, G. E. (1995). Reduction in sensorimotor control with age. *Quest, 47*(3), 386-394.

Seidler, R. D., Alberts, J. L., & Stelmach, G. E. (2002). Changes in multi-joint performance with age. *Motor control, 6*(1), 19-31.

Seidler, R. D., Bernard, J. A., Burutolu, T. B., Fling, B. W., Gordon, M. T., Gwin, J. T., ... & Lipps, D. B. (2010). Motor control and aging: links to age-related brain structural, functional, and biochemical effects. *Neuroscience & Biobehavioral Reviews, 34*(5), 721-733.

Seidler, R. D., Bo, J., & Anguera, J. A. (2012). Neurocognitive contributions to motor skill learning: the role of working memory. *Journal of motor behavior*, *44*(6), 445-453.

Shadlen, M.N., Movshon, J.A. (1999). Synchrony unbound: review a critical evaluation of the temporal binding hypothesis. *Neuron, 24*:67–77.

Shallice, T., Fletcher, P., Frith, C. D., Grasby, P., Frackowiak, R. S. J., & Dolan, R. J. (1994). Brain regions associated with acquisition and retrieval of verbal episodic memory. *Nature*, *368*(6472), 633-635.

Shemmell, J., Forner, M., Tathem, B., Tresilian, J. R., Riek, S., Barry, B. K., & Carson, R. G. (2006). Neuromuscular-skeletal constraints on the acquisition of skill in a discrete torque production task. *Experimental Brain Research*, *175*(3), 400–410. http://doi.org/10.1007/s00221-006-0547-y

Shemmell, J., Forner, M., Tresilian, J. R., Riek, S., Barry, B. K., & Carson, R. G. (2005a). Neuromuscular adaptation during skill acquisition on a two degree-of-freedom target-acquisition task: isometric torque production. *Journal of Neurophysiology*, *94*(5), 3046–3057. http://doi.org/10.1152/jn.00670.2004

Shemmell, J., Tresilian, J. R., Riek, S., Barry, B. K., & Carson, R. G. (2005b). Neuromuscular adaptation during skill acquisition on a two degree-of-freedom target-acquisition task: dynamic movement. *Journal of Neurophysiology*, *94*(5), 3058–3068. http://doi.org/10.1152/jn.00671.2004

Shepard, R. N., & Metzler, J. (1971). Mental rotation of three-dimensional objects. *Science*, *171*(3972), 701-703.

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective?. *Psychological bulletin*, *138*(4), 628.

Shumway-Cook, A., Patla, A. E., Stewart, A., Ferrucci, L., Ciol, M. A., & Guralnik, J. M. (2002). Environmental demands associated with community mobility in

older adults with and without mobility disabilities. *Physical therapy*, *82*(7), 670-681.

Sibley, B. A., & Etnier, J. L. (2003). The relationship between physical activity and cognition in children: a meta-analysis. *Pediatric exercise science*, *15*(3), 243-256.

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. L. (2016). Do "Brain-Training" Programs Work? *Psychological Science in the Public Interest, 17*(3), 103–186. http://doi.org/10.1177/1529100616661983

Singer, W.(2001). Consciousness and the binding problem. *Ann N Y Acad Sci., 929*(1):123–46.

Sleimen-Malkoun, R., Temprado, J. J., & Berton, E. (2013). Age-related dedifferentiation of cognitive and motor slowing: insight from the comparison of Hick--Hyman and Fitts' laws. *Frontiers in aging neuroscience, 5*.

Smith, P. J., Blumenthal, J. A., Hoffman, B. M., Cooper, H., Strauman, T. A., Welsh-Bohmer, K., ... & Sherwood, A. (2010). Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. *Psychosomatic medicine*, *72*(3), 239.

Snodgrass, J. G., & Corwin, J. (1988). Pragmatics of measuring recognition memory: Applications to dementia and amnesia. *Journal of Experimental Psychology: General, 117*(1), 34 50.

Souders, D. J., Boot, W. R., Blocker, K., Vitale, T., Roque, N. A., & Charness, N. (2017). Evidence for Narrow Transfer after Short-Term Cognitive Training in Older Adults. *Frontiers in Aging Neuroscience, 9*, 366–10. http://doi.org/10.3389/fnagi.2017.00041

Sowell, E. R., Peterson, B. S., Thompson, P. M., Welcome, S. E., Henkenius, A. L., & Toga, A. W. (2003). Mapping cortical change across the human life span. *Nature neuroscience*, *6*(3), 309-315.

Spiegel, M. A., Koester, D., & Schack, T. (2013). The functional role of working memory in the (re-) planning and execution of grasping movements. *Journal of Experimental Psychology: Human Perception and Performance, 39*(5), 1326.

Spiegelhalter, D. J., Best, N. G., Carlin, B. P., & Van Der Linde, A. (2002). Bayesian measures of model complexity and fit. *Journal of the Royal Statistical Society: Series B (Statistical Methodology), 64*(4), 583-639.

Spirduso, W. W. (1975). Reaction and movement time as a function of age and physical activity level. *Journal of Gerontology*, *30*(4), 435-440.

Spirduso, W. W., & MacRae, P. G. (1990). Motor performance and aging. *Handbook of the psychology of aging, 3*, 183-200.

Spirduso, W. W., Francis, K. L., & MacRae, P. G. (1995). *Physical dimensions of aging*.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *J. Int. Neuropsychol. Soc., 8*, 448–460.

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia*, *47*(10), 2015-2028.

Stern, Y., Gurland, B., Tatemichi, T. K., Tang, M. X., Wilder, D., & Mayeux, R. (1994). Influence of education and occupation on the incidence of Alzheimer's disease. *Jama, 271*(13), 1004-1010.

Stevenson, H., Russell, P. N., & Helton, W. S. (2011). Search asymmetry, sustained attention, and response inhibition. *Brain and cognition*, *77*(2), 215-222.

Stout, D. (2010). The evolution of cognitive control. *Topics in Cognitive Science*, *2*(4), 614-630.

Stuss, D. T., Levine, B., Alexander, M. P., Hong, J., Palumbo, C., Hamer, L., ... & Izukawa, D. (2000). Wisconsin Card Sorting Test performance in patients with focal frontal and posterior brain damage: effects of lesion location and test structure on separable cognitive processes. *Neuropsychologia, 38*(4), 388-402.

Tang, P. F., & Woollacott, M. H. (1996). Balance control in older adults: Training effects on balance control and the integration of balance control into walking. *Advances in Psychology, 114*, 339-367.

Tardif, S., & Simard, M. (2011). Cognitive stimulation programs in healthy elderly: a review. *International Journal of Alzheimer's Disease, 2011*, 378934.

Taubert, M., Lohmann, G., Margulies, D. S., Villringer, A., & Ragert, P. (2011). Long-term effects of motor training on resting-state networks and underlying brain structure. *Neuroimage*, *57*(4), 1492-1498.

Taylor, J. A., & Ivry, R. B. (2014). Cerebellar and prefrontal cortex contributions to adaptation, strategies, and reinforcement learning. *Progress in brain research*, *210*, 217.

Taylor, J., & Thoroughman, K. (2007). Divided attention impairs human motor adaptation but not feedback control. *J Neurophysiol, 98*(1), 317-326.

Taylor, J., & Thoroughman, K. (2008). Motor adaptation scaled by the difficulty of a secondary cognitive task. *PLoS ONE* 3: e2485.

Teasdale, N., Bard, C., Fleury, M., Young, D. E., & Proteau, L. (1993). Determining movement onsets from temporal series. *Journal of motor behavior*, *25*(2), 97-106.

Theeuwes, J. (2010). Top–down and bottom–up control of visual selection. *Acta psychologica*, *135*(2), 77-99.

Tomporowski, P. D., McCullick, B., Pendleton, D. M., & Pesce, C. (2015). Exercise and children's cognition: the role of exercise characteristics and a place for metacognition. *Journal of Sport and Health Science*, *4*(1), 47-55.

Toril, P., Reales, J. M., Mayas, J., & Ballesteros, S. (2016). Video Game Training Enhances Visuospatial Working Memory and Episodic Memory in Older Adults. *Frontiers in Human Neuroscience, 10*, 753–14. http://doi.org/10.3389/fnhum.2016.00206

Trewartha, K. M., Garcia, A., Wolpert, D. M., & Flanagan, J. R. (2014). Fast but fleeting: adaptive motor learning processes associated with aging and cognitive decline. *The Journal of Neuroscience, 34*(40), 13411-13421.

Tseng, Y. W., Diedrichsen, J., Krakauer, J. W., Shadmehr, R., & Bastian, A. J. (2007). Sensory prediction errors drive cerebellum-dependent adaptation of reaching. *Journal of neurophysiology*, *98*(1), 54-62.

Tupper, D., and Cicerone, K. (1990). Introduction to the neuropsychology of everyday life. In: Tupper, D., and Cicerone, K. (eds.), *The Neuropsychology of Everyday Life: Assessment and Basic Competencies,* Kluwer Academic, Boston, MA, pp. 3-18.

UN World Population Ageing (2015). Retrieved from http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf. United Nations, New York.

Uttal, W. R. (2013). *Reliability in cognitive neuroscience: a meta-meta-analysis*. MIT Press.

Vallesi, A., McIntosh, A. R., & Stuss, D. T. (2011). Overrecruitment in the aging brain as a function of task demands: evidence for a compensatory view. *Journal of Cognitive Neuroscience*, *23*(4), 801-815.

Vallortigara, G., Rogers, L. J., & Bisazza, A. (1999). Possible evolutionary origins of cognitive brain lateralization. *Brain Research Reviews, 30*(2), 164-175.

Van Donkelaar, P., & Franks, I. M. (1991). Preprogramming vs. online control in simple movement sequences. *Acta psychologica,* 77(1), 1-19.

Vera, A. H., & Simon, H. A. (1993). Situated action: A symbolic interpretation. *Cognitive Science*, *17*, 7–48.

Verhaeghen P, Basak C. (2005). Ageing and switching of the focus of attention in working memory: results from a modified N-back task. *The Quarterly Journal of Experimental Psychology, 58*:134–54.

Voelcker-Rehage, C., & Niemann, C. (2013). Structural and functional brain changes related to different types of physical activity across the life span. *Neuroscience & Biobehavioral Reviews*, *37*(9 Pt B), 2268–2295. http://doi.org/10.1016/j.neubiorev.2013.01.028

Voelcker-Rehage, C., & Wiertz, O. (2003). *Die Lernfähigkeit sportmotorischer Fertigkeiten im Lichte der Entwicklungspsychologie der Lebensspanne* (Doctoral dissertation).

Voelcker-Rehage, C., Godde, B., & Staudinger, U. M. (2010). Physical and motor fitness are both related to cognition in old age. *European Journal of Neuroscience, 31*(1), 167-176. http://doi.org/10.1111/j.1460-9568.2009.07014.x

Voelcker-Rehage, C., Godde, B., and Staudinger, U. M. (2010). Cardiovascular and motor fitness are both related to cognition in old age. *Eur. J. Neurosci. 31*, 167--176.

Voelcker-Rehage, C., Godde, B., Staudinger. U. M. (2011). Cardiovascular and coordination training differentially improve cognitive performance and neural processing in older adults. *Front Hum Neurosci, 17*(5):26.

Wagner, G. P., & Trentini, C. M. (2009). Assessing executive functions in older adults: A comparison between the manual and the computer-based versions of the Wisconsin Card Sorting Test. *Psychology & Neuroscience, 2*(2), 195.

Wang, H., Karp, A., Winblad, B., Fratiglioni, L. (2002). Late life engagement in social and leisure activities is associated with a decreased risk of dementia: A longitudinal study from the Kungsholmen project. *American Journal of Epidemiology* , 155,1081-1087.

Welford, A. T. (1988). Reaction time, speed of performance, and age. *Annals of the New York Academy of Sciences, 515*(1), 1-17.

West, R. L. (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychological bulletin, 120*(2), 272.

Wilcox, R. (2012). *A Foundation for Robust Methods*. Third Edition. Elsevier Inc.

Wilhelm, O., Hildebrandt, A., & Oberauer, K. (2013). What is working memory capacity, and how can we measure it?. *Frontiers in psychology*, *4*.

Wilson, George and Shpall, Samuel, "Action", *The Stanford Encyclopedia of Philosophy* (Winter 2016 Edition), Edward N. Zalta (ed.), URL = <https://plato.stanford.edu/archives/win2016/entries/action/>.

Wolpert, D., & Ghahramani, Z. (2000). Computational principles of movement neuroscience. *Nat Neurosci, 3 Suppl*, 1212-1217.

Wolpert, D.M., Miall, R.C., and Kawato, M (1998). Internal models in the cerebellum. *Trends in cognitive sciences 2*: 338-347.

Wyss, R., König, P., & Verschure, P. F. (2004). Involving the motor system in decision-making. *Proceedings of the Royal Society of London B: Biological Sciences*, *271*(Suppl 3), S50-S52.

Yaffe, K., Fiocco, A. J., Lindquist, K., Vittinghoff, E., Simonsick, E. M., Newman, A. B., ... & Harris, T. B. (2009). Predictors of maintaining cognitive function in older adults: The Health ABC Study. *Neurology*, *72*(23), 2029-2035.

Yan, J. H. (2000). The effects of aging on linear and curvilinear arm movement control. *Experimental Aging Research*, 26, 393–407.

Yan, J. H., Thomas, J. R., & Stelmach, G. E. (1998). Aging and rapid aiming arm movement control. *Experimental Aging Research*,*24*,55- 69.

Yan, J. H., Zhou, C.L. (2009). Effects of motor practice on cognitive disorders in older adults. *Eur Rev Aging Phys Act, 6*(2):67-74.

Young, J., Angevaren, M., Rusted, J., & Tabet, N. (2015). Aerobic exercise to improve cognitive function in older people without known cognitive impairment. *The Cochrane Library*.

Zelinski, E. M., Peters, K. D., Hindin, S., Petway, K. T., and Kennison, R. F. (2014). Evaluating the relationship between change in performance on training tasks and on untrained outcomes. *Front. Hum. Neurosci.* 8:617. doi: 10.3389/fnhum. 2014.00617

Appendices

Appendix 1.

Table 5.1 Appendix 1 Mean Reaction Time for each Training Day in the Visuomotor Training Task, and contrasts with Day 1 scores.

Time	**Mean (SE)**	**95% Confidence Intervals** *(lower bound, upper bound)*	**Contrast with Day 1** *(p-value)*
Day1	0.407 (.013)	0.382, 0.431	-
Day2	0.405 (.013)	0.380, 0.430	0.810
Day3	0.410 (.013)	0.385, 0.434	0.620
Day4	0.403 (.013)	0.378, 0.428	0.531
Day5	0.405 (.013)	0.380, 0.430	0.758

Appendix 2

Table 5.2 Pre-post and pre-retention contrasts for Reaction Time on the Baseline Visuomotor Task: Training and Control Groups

		Training			**Control**		
Hand	Target	Lsmean (pre)	Lsmean (post)	*p-value*	Lsmean (pre)	Lsmean (post)	*p-value*
Left	***flx***	0.439 (0.16)	0.403 (0.16)	0.013*	0.413 (0.14)	0.398 (0.14)	0.247
	flx_rad	0.438 (0.16)	0.391 (0.15)	0.001*	0.437 (0.15)	0.405 (0.15)	0.014*
	rad	0.434 (0.15)	0.387 (0.16)	0.002*	0.414 (0.15)	0.402 (0.15)	0.390
	ext_rad	0.441 (0.16)	0.381 (0.15)	0.000*	0.426 (0.15)	0.397 (0.15)	0.024*
	ext	0.438 (0.15)	0.385 (0.16)	0.000*	0.423 (0.14)	0.390 (0.15)	0.011*
	ext_uln	0.422 (0.15)	0.403 (0.16)	0.191	0.422 (0.15)	0.431 (0.14)	0.504
	uln	0.434 (0.15)	0.401 (0.16)	0.023*	0.429 (0.15)	0.428 (0.14)	0.925
	flx_uln	0.415 (0.15)	0.400 (0.16)	0.269	0.427 (0.15)	0.404 (0.14)	0.082
Right	***flx***	0.403 (0.16)	0.381 (0.16)	0.152	0.397 (0.15)	0.391 (0.15)	0.641
	flx_rad	0.428 (0.16)	0.376 (0.16)	0.000*	0.433 (0.15)	0.406 (0.15)	0.040*
	rad	0.425 (0.16)	0.398 (0.16)	0.068	0.442 (0.15)	0.426 (0.15)	0.210
	ext_rad	0.433 (0.16)	0.395 (0.16)	0.009*	0.422 (0.15)	0.439 (0.15)	0.192
	ext	0.403 (0.16)	0.387 (0.16)	0.260	0.415 (0.16)	0.424 (0.15)	0.507
	ext_uln	0.405 (0.16)	0.398 (0.16)	0.616	0.433 (0.15)	0.425 (0.15)	0.530
	uln	0.443 (0.16)	0.413 (0.16)	0.041*	0.444 (0.15)	0.439 (0.15)	0.763
	flx_uln	0.428 (0.16)	0.388 (0.16)	0.007*	0.426 (0.15)	0.419 (0.14)	0.575